THE EFFECT OF DISEASE ON THE TIME CONSTANT OF ACCOMMODATION IN PERIPHERAL NERVE

A thesis

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Last but not least, I must express my gratitude to the patients who offered themselves as the subjects for the investigation; the work would not have been possible without their co-operation.

PREFACE

No reports on the effect of diseases of the lower motor neurone on the accommodation in peripheral nerve could be found in the literature. Hence it was thought worthwhile to study this aspect in human subjects, which is the theme of the present thesis. The work embodied in this thesis was carried out in the Department of Neurology, University of Edinburgh from 1st October 1962 to 30th September 1964, under the supervision of Dr. J.A. Simpson and with a grant from the Scottish Hospital Endowments Research Trust, which is gratefully acknowledged.

The author regrets that a larger number of subjects could not be included in the present study, but one must accept the limitations inherent in using human subjects, especially the sick, as material for research. Availability of patients with particular disease states varies from time to time. The patients' fitness to undergo the study and their readiness to submit themselves to this examination have also to be considered.

The examination was carried out with the consent of the person concerned, after it had been explained that this particular examination was entirely a research procedure and in the present state of our knowledge was unlikely to help in the diagnosis or treatment of his or her disease.

'True science suppresses nothing, but goes on searching and is undisturbed in looking straight at things that it does not yet understand.'

Claude Bernard (1927)

CHAPTER 1

INTRODUCTION

Definition of the term accommodation

An electric current which rises to its full value instantly is a more effective stimulus and excites a nerve fibre at a lower strength than one which rises slowly. Nernst (1908) mamed this ability of a nerve fibre to set up a resistance against a slowly rising current as 'accommodation'. Such a property of accommodation has been observed in other tissues like muscles and nerve cells also. In this thesis, the term will be used to refer to this property in peripheral nerves unless otherwise specified.

Evolution of the present knowledge on accommodation

In the course of his pioneering work on the electrophysiology of nerves, du Bois Reymond (1862) attempted unsuccessfully to study the effect of a slowly rising current on the nerve fibre. In 1877, v. Fleischl reported that a current causing excitation of a nerve fibre when rising instantly was ineffective if reached slowly. In 1884, von Kries reported that the current had to be stronger to become an effective stimulus if the rate of its rise was diminished. He obtained an 'excitation quotient' by dividing the threshold voltage of a linearly rising current by that of an instantly rising current. He also published curves relating effective strengths to rising times of stimulating currents. However, he failed to obtain consistent results with his method. Lucas (1907) postulated that the stimulating current must have a minimal rising gradient to excite a toad or frog nerve; one having a lower gradient would be unable to excite.

Fabre(1927, 1928) studied the relationship between the threshold current strength necessary to stimulate a nerve fibre and the time taken to reach the threshold. He used the term 'constante lineaire' to denote the reciprocal of the minimal current gradient necessary for stimulation of a nerve fibre. Schriever (1930, 1932) coined the word 'Einschleichzeit' (Einschleichen - to creep; zeit - time) to indicate the time constant of accommodation. He determined the time constant of rise for an exponential current which just excited a nerve at twice the rheobase; the utilisation time or 'halb-zeit' (0.693a where a is the time constant of current rise) for this current was 'Einschleichzeit'. Lapique (1937) studied the effect of an exponentially rising current of rheobasic strength, the rise time of such a current which was just unable to excite, was termed by him as the 'seuil de climalyse'. He proposed its use for the quantitative expression of accommodation. Rashevsky (1934) in a mathematical approach to the problem of nerve stimulation commented that a slowly rising or falling current can not excite a nerve within certain limits of strength. Monnier (1934) mentioned a time constant τ_2 in his mathematical study of nerve excitation. This is similar to the time constant of accommodation. Hill (1936) used the term λ for the quantitative expression of the time constant of accommodation.

Parrack (1940) on the other hand, working with frog nerves, concluded that a nerve shows accommodation only when its circulation is interfered with and that accommodation is not a feature of a nerve with intact circulation. I could not find any other work confirming this conclusion excepting that of Schoepfle (1943). Schoepfle obtained absence of accommodation in some of the fibres of frog toe nerve, but accommodation was detectable in some of the other fibres of the same nerve. In addition, for all the fibres he found that stimulation failed to occur below a minimal gradient of current.

Sato (1951-52) detected a smaller accommodation in single fibres of toad nerve than in the whole nerve. He explained that the difference was due to the distortion of the applied current by the conductivity of the connective tissue covering of the whole nerve. Solandt (1936), however, failed to observe alteration of accommodation after desheathing.

It is also worth mentioning that a difference exists between the capacity of accommodation of sensory nerve fibres and that of motor fibres. Sensory fibres have been observed to have a lower accommodation than motor ones; the breakdown of accommodation also occurs earlier in the former (Skoglund, 1942; Kugelberg, 1944).

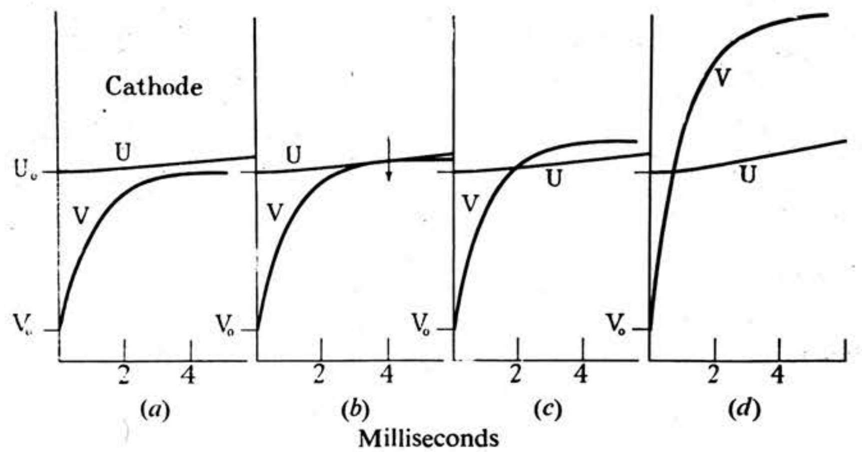
Alteration of accommodation in animals

Lucas (1908) showed that the accommodation of muscle was impaired if the bathing fluid lacked calcium and that this impairment could be corrected by adding calcium chloride. Kahn (1911) confirmed this deleterious effect of calcium lack on muscle accommodation. Solandt (1936) observed a similar effect of calcium on nerve accommodation. He, in the same study, also noted that alkalinity of the bathing fluid impaired and acidity increased the capacity of accommodation in the nerves. Liesse (1938a, b) reported an increased accommodation in ischaemic nerves. Cold, drying or mechanical injury to the nerve was shown to produce the opposite effect (Schriever and Cebulla, 1938).

Flattening of the accommodation curve was noted by L. & M. Lapique (1937) and by P. & M. Benoit (1937) in states of cold and decalcification. Tasaki (1949) observed deterioration of accommodation with lowering of temperature. Alteration of accommodation by some narcotics has been reported (Kahlson and v. Werz, 1936; Schriever and Erhardt, 1939). Excess of other ions like magnesium, potassium and strontium was found to increase the degree of accommodation (Solandt, 1936). Sato et al (1950-51) reported reduction of accommodation in single nerve fibres by the actions of veratrine, quinidine and aconitine. Hypertonic saline (Sato, 1950-51 a) and tetraethyl ammonium iodide (Cowan and Walter, 1937-38) were observed to have a similar effect.

Physiological basis of accommodation

Hill (1936) postulated that the excitation of a nerve fibre occurs when the local potential V_0 equals threshold value U_0. During stimulation V_0 is assumed to rise at a rate proportional to I_0, the applied current. If, however, a slowly rising current is applied, the threshold at the cathode rises due to the action of the subthreshold current at the initial part of the rising current and reaches a new higher value U. As a result, to produce an excitation, the



(*a*) current = 1, (*b*) current = 1·08, (*c*) current = 1·2, (*d*) current = 2·0

Rise of " local potential " V and of " threshold " U, at the cathode, for constant current suddenly applied. Calculated for frog's nerve at 4° C, ordinary " accommodation," $k = 1$, $\lambda = 50$ m sec: various currents, as shown. Current 1 would be " rheobase " apart from accommodation. The actual rheobase is 1·08, and its " utilization time " is shown by an arrow.

FIG. 1

FIGURE 1

The outline of Hill's hypothesis on the physiological basis of accommodation in a nerve is shown diagrammatically (Reproduced from Hill (1936)).

slowly rising current has to be stronger to raise the local potential to correspond to the raised threshold. When the slowly rising stimulus is withdrawn, the threshold reverts to normal over an exponential time constant. He named this time constant of reversion to normality as λ and considered it as the time constant of accommodation (vide fig. 1). His theory can be expressed mathematically in a simplified form as $\frac{-dU}{dt} = \frac{U-U_0}{\lambda}$ (dU being the rate of change of local threshold). Rashevsky (1936) in his theory of nerve excitation, conceived a rapid excitatory process and a slow inhibitory process expressed as e and i respectively. Each varies with the current according to the equations $\frac{de}{dt} = KI - k(e-e_0)$ and $\frac{di}{dt} = MI - m(i-i_0)$ K, k, M, m are constant and e_0 and i_0 are the initial values of e and i and I the current. Excitation occurs, according to him, when e/i reaches a critical threshold value. Katz (1939) described accommodation as the effect of a process which, under the influence of a constant stimulus, tends to re-establish the normal unstimulated condition in the nerve. Lorrente de Nó (1947) holds a somewhat similar view. According to him, accommodation is due to the tendency of the nerve to re-establish equilibrium against the applied current. This reaction of the nerve removes a fraction of the stimulus from a slowly rising current, as the initial part of this current

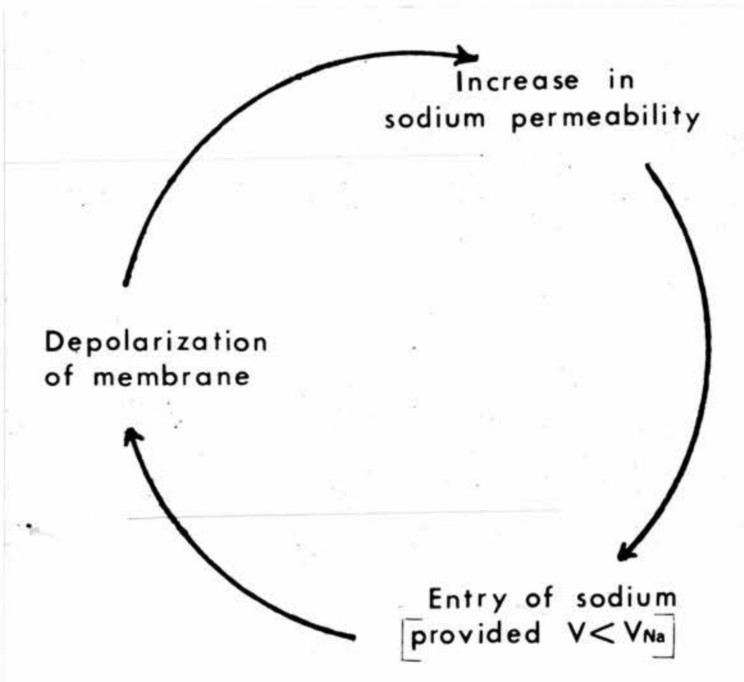

Increase in sodium permeability
Entry of sodium [provided V< VNa]
Depolarization of membrane

FIG.2

FIGURE 2

Shows diagrammatically the linking of sodium permeability and membrane potential as suggested by Hodgkin (Reproduced from Hodgkin (1964)).

is subthreshold. Consequently a current rising slowly needs an increased strength to stimulate. Hodgkin (1964) is of the opinion that not enough work has yet been done to explain the mechanism fully. He has, however, put forward a possible hypothesis as the basis of accommodation. He suggests that, when a nerve membrane is depolarised, its permeability to sodium increases. The sodium permeability and the membrane potential are, according to his theory, linked 'regeneratively' in the manner shown in fig. 2. Due to this linkage, sodium ions enter the fibre at an increased rate when the membrane has been depolarised beyond a certain critical point. This rapid entry of sodium moves the membrane potential rapidly towards the equilibrium potential of the sodium ion. The threshold for the production of an action potential is the degree of membrane depolarisation at which the inward sodium current just balances the outward potassium current. In addition to the rapid effect of membrane depolarisation mentioned above, Hodgkin maintained that there is also a slow effect which inactivates the sodium carrying system and raises the potassium permeability. If the depolarisation is gradual, the slow effect predominates and blocks the regenerative action of the increase in sodium permeability. As the threshold is the potential at which the inward sodium current just balances the outward potassium current, with a slowly rising current most nerves pass into a refractory state without giving an action potential.

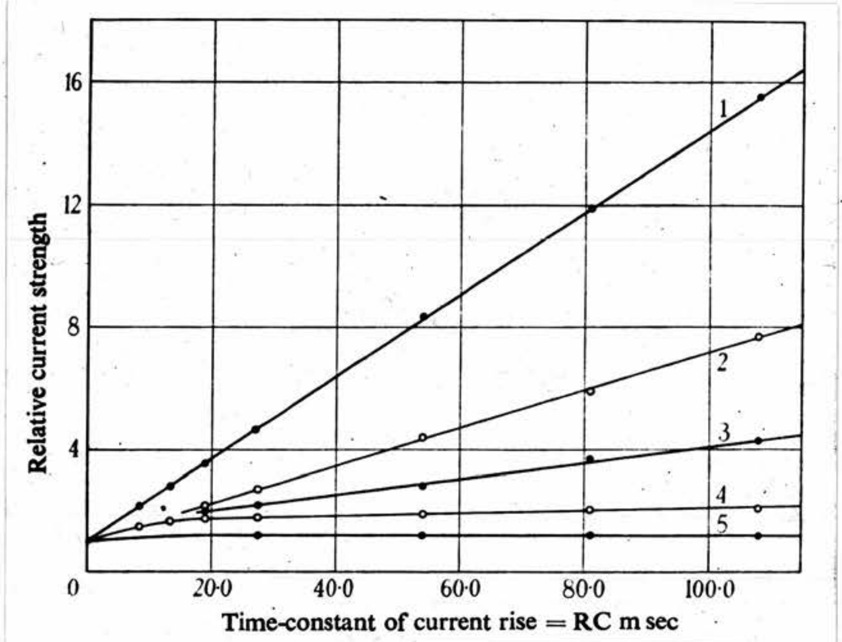
Whatever the explanation, all workers agree that the accommodation of peripheral nerves is associated with the 'sodium pump', or the possible inactivation of the 'potassium pump' and requires the presence of calcium ions (Hodgkin, 1964). These 'pumps' require metabolic energy and so are vulnerable to disorders affecting the energy metabolism of the excitable cell (Simpson, 1962a,b). This metabolism is oxidative (Shanes & Berman, 1956; Connelly, 1959). The dependence of accommodation on some forms of oxidative metabolism is further suggested by the alteration of accommodation in states of ischaemia and with changes in the pH of the environment and by the effects of ionic changes and of drugs. Solandt (1936) suggested a possible correlation between the rate of destruction of an acetylcholine-like substance and the time constant of accommodation. This acetylcholine-like substance is thought by Nachmansohn (1959) to be produced during the passage of a nerve impulse, but the majority of workers do not accept this mechanism.

Mechanism of action of calcium on nerve accommodation

The calcium ion influences the phenomenon of accommodation markedly (vide pp 4 and 13), but the exact basis of the relationship between the two is still disputed. Hodgkin, Huxley & Katz (1949) suggested that calcium influences the excitability of a nerve by its reaction with organic ions which are required for transport of sodium ions across the cell membrane. Shanes (1949 a, b) maintained that calcium acts on the molecules controlling the permeability of the membrane for potassium and thus controls the excitability of a nerve. Brink (1954) has postulated that, as a result of its action on the ion transport across the nerve surface, calcium modifies the tendency of the membrane potential to oscillate during current flow. None of these theories have been accepted universally.

Quantitative expression of accommodation

Hill (1936) observed that the phenomenon studied by different experimental methods can be expressed by the same constant and proved that Fabre's 'constante lineaire' (1927), Schriever's (1932)'Einschleichzeit' (multiplied by 2,89) and Monnier's τ_2 are the same as λ. Hill further concluded that the ratio of the threshold



16
12
8
4
0
Relative current strength
1
2
3
4
5
20·0
40·0
60·0
80·0
100·0
Time-constant of current rise = RC m sec

FIG. 3

FIGURE 3

Shows the relationship between the slope of accommodation curve and . (1) - λ = 7.4m. sec.; (2) - λ = 16.1m.sec. (3) - λ = 39.0m.sec.; (4) - λ = 260m.sec.; (5) - λ = ∞ (Reproduced from Solandt (1936)).

exponential current (I) to the rheobase for a current of instantaneous onset (I_0) should bear a linear relationship to the time constant of current rise and that the slope of this line should equal the reciprocal of the time constant of accommodation ($1/\lambda$). Accordingly the lower the capacity for accommodation the higher the λ and viceversa (vide fig. 3). He recommended the use of the reciprocal of the slope as a measurement of accommodation. The simplest way of obtaining this lime is to determine the rheobase with a current pulse which has an instantaneous rise and then to obtain the threshold for stimulation for current pulses rising exponentially with different time constants. The various thresholds obtained in this manner are plotted in terms of their ratio to the rheobase of the instantaneous current. The ratio is a better index of stimulus strength as an absolute value may vary with tissue impedance. The time constants are plotted as abscissa and the relative current strengths as ordinate. Instead of an exponentially rising current, a linearly rising current can be used in the same manner.

In addition to the use of progressive current as in the method mentioned above, measurement of galvanic-tetanus ratio and alternating current intensity -

frequency curves can also be used to demonstrate the presence of accommodation (Ritchie, 1954), but these methods are less quantitative than the method just described.

Nature of accommodation Curve

Solandt (1935, 1936) in his experiments on animals and human subjects confirmed the linearity of accommodation curves as predicted by Hill (1936). Among the earlier workers, Cardot and Laugier (1913) using frog sciatic nerve, obtained good straight lines by plotting absolute thresholds against time constants of current rise with slowly rising currents. Schriever (1930) and Delville (1934) also obtained straight lines by similar plotting.

However, it was observed by Bernhard et al (1942) that the accommodation curve, although linearly rising in the initial part, tended to become relatively horizontal when the strengths of the slowly rising currents were sufficiently great. These workers pointed out that the nerve could accommodate itself against slowly rising currents within a certain range of current strength only and that beyond this point there was a breakdown or impairment of accommodation. This breakdown of accommodation has been found to occur at

2.5 - 5 times the rheobasic current (Kugelberg, 1944).

In view of this breakdown of accommodation at a certain stage, Whitteridge (1950) has doubted the dependence of accommodation on a single factor as suggested by Hill (1936).

Previous studies on the phenomenon in man

Normal : In common with most other neurophysiological problems, accommodation has largely been studied in animal preparations. The present work is concerned with this feature of nervous excitability in humans and so a discussion of previous studies in man is appropriate.

Fabre's (1928) paper was possibly the first report on this aspect with a quantitative determination of 'constante lineaire' in normal individuals. Later, Liberson (1934) published a few normal accommodation curves. Schriever (1932) determined his 'Einschleichzeit' at the motor point of Biceps in six normal individuals. Solandt (1935, 1936) and Granit and Skoglund (1942) reported their observations on a limited number of normal subjects.

Kugelberg (1944) has published the largest series of observations so far reported in normal individuals. He determined the accommodation in the ulnar nerve of one hundred normal individuals. In his paper, he constructed accommodation curves by the method of Hill (1936), but he expressed the capacity of accommodation in terms of the actual slope of the initial linear part of the curve instead of its reciprocal. His observations on the initial linearity were in agreement with those of previous workers (Solandt, 1936; Hill, 1936); he also noted the breakdown of accommodation when the current was sufficiently strong as mentioned by Bernhard et al (1942). Kugelberg's studies included comparisons between the time constants of accommodation of different nerves in the same individual as well as of the long and short fibres of the ulnar and median nerves. His conclusions will be discussed in more detail in a later chapter. Simpson (1955) reported his observations on the time constant of accommodation in the ulnar nerve in 32 normal subjects.

Abnormal : Kugelberg (1944) also observed the effects of calcium deficiency and ischaemia on accommodation. Both these conditions were found to lower the property of accommodation. Solandt(1936) and Wigton & Brink (1944) also noted impaired accommodation in hypocalcaemic subjects. These observations were confirmed by Simpson (unpublished personal communication) who has also detected decreased accommodation of nerves in a hypothermic subject (1955) and increased accommodation in hypercalcaemic states (Simpson, 1954). The effects of cold and calcium deficiency on human nerve accommodation are in agreement with those observed in animals (vide p. 4).

Accommodation and repetitive responses in the nerve

In a state of decreased accommodation, a nerve has a tendency to fire repetitively when stimulated by stimuli near threshold intensity (Katz, 1937). Spontaneous firing has also been reported in animal and human nerves with lowered accommodation (Katz, 1937; Schriever & Cebulla, 1938) causing twitching or tetanic spasm of muscle if motor fibres were affected, or paraesthesia if sensory fibres fired spontaneously (Kugelberg, 1944). A phenomenon of this nature could account for the paraesthesia associated with certain diseases of the peripheral nerves. Simpson (1956) noted a tendency for repetitive responses to stimulation by brief electrical shocks in compressed nerves as in the carpal tunnel syndrome.

Purpose of the present study

From the above review, it is evident that the property of accommodation in peripheral nerves in man has received little attention, particularly in pathological states. As the property of a peripheral nerve to accommodate to slowly rising currents depends upon oxidative metabolism, unlike the velocity of conduction (Simpson, 1962a,b), it was thought worthwhile to study this phenomenon and its correlation with the clinical or other electrical alterations in the peripheral nerves of patients suffering from various diseases affecting mainly the lower motor neurone.

The value of measuring the accommodation in the diagnosis of peripheral nerve injuries has been stressed by Ritchie (1954), but there have been no reports on this, using the full method described in this thesis. 'Accommodation Index', which depends on the phenomenon of accommodation was never observed to be less than 4 in normal muscles (Ritchie, 1954) whereas in denervated muscles it approached unity, indicating a lowering of the property of accommodation (Pollock et al, 1944, 1945). Pollock et al (1944, 1945) measured accommodation by stimulating motor points. Kugelberg (1944) has shown the limitations of using stimulation at such sites in the measurement of accommodation.

The measurement of nerve accommodation by using progressive currents in the diagnosis of peripheral nerve lesions is, however, unlikely to be adopted as a routine procedure. Stimulation by a slowly rising current is more painful to the subjects than stimulation by an instantly rising one and a number of such stimuli are needed to draw an accommodation curve. Consequently many patients may not agree to submit to such a procedure. Moreover, the test is time consuming, being more suitable for special studies than for routine investigations. Use of other methods for measurement such as the determination of the galvanic-tetanus ratio and alternating current intensity-frequency curves are also hazardous for the subjects (Ritchie, 1954).

<u>Scope of the present study</u>

In this study, accommodation was measured in the motor fibres of different peripheral nerves. The study was carried out on a group of controls and on patients with compression neuropathies, motor neurone disease (amyotrophic lateral sclerosis) and polyneuropathy.

CHAPTER 2

METHOD

Stimulator

Most of the workers in the field of accommodation have used stimulators producing progressive currents. These stimulators can be divided in two main groups :

1) Those producing exponentially rising current and
2) those producing linearly rising current.

Gildmeister (1904), Lapique (1926), Schriever (1930), Solandt (1936), Kugelberg (1944) among others have used the former type of stimulator in their studies and v. Kries (1884), Lucas (1907), Blair (1935), Fabre (1927) on the other hand, have used the latter type.

Skoglund (1942) has advocated the use of linearly rising current in preference to exponential for studies on accommodation, but Landolt (1942) commented that interpretation of values obtained by linearly rising current was more difficult. Hill (1936) has shown that comparable values for the time constant of accommodation could be achieved by using either exponentially or linearly rising current.

For the present study exponentially rising current has been used to measure accommodation. This form of stimulation has been selected as most of the studies on human subjects available for comparison have been carried out with this form of current.

A constant current stimulator was employed for this study. It was built in the Institute of Neurology, Queen Square, London, adopting the circuit described by Andrew (1952) with slight modifications. The stimulator could be set to give either an abrupt rise of current or an exponential rise according to the equation $I = I_0 \quad (1 - e^{-t/a})$ where I_0 = final current, e = Naperian logarithmic base, a = time constant of current and t = time.

The current output and the time constant could be varied independently in the stimulator.

The time constant could be adjusted by a switch, which controlled the value of capacitance to produce current rise of preset time constants ranging from 0 to 250 milliseconds in steps of 25 milliseconds.

By changing the value of the series resistance in the output stage, the stimulator could be adjusted to give a predetermined current output from 0.1 mA to 10 mA. in steps of 0.1 mA. The high source impedance of the output stage of the stimulator allowed the output current to be practically independent of the patient's resistance. The same factor also made the time constant independent of patient's resistance. The duration of the applied current was fixed at 3 secs.

FIG. 4

FIGURE 4

Shows the experimental set up for stimulating the ulnar nerve at elbow (see text for details).

Electrodes

A one centimetre diameter lint-covered silver-silver chloride electrode was used as the cathode and a broad thin copper plate wrapped in a piece of lint was used as the anode. For the experiments, the electrodes were thoroughly soaked with normal saline before use and Cambridge electrode jelly was rubbed on the skin of the patients at the site of application of the electrodes until an erythema was produced to minimise skin resistance.

Experimental procedure

Position of the subject : The subjects sat at a table opposite the experimenter when the nerves of the upper limbs were being investigated and lay on a table for the study of the nerves of the legs.

Set up for studying ulnar and median nerves : For investigation of the ulnar nerve, the cathode was placed over the nerve at the olecranon fossa at the elbow. The anode was placed over the ventral aspect of the forearm. The electrodes were fixed firmly in position with straps and the subjects were asked to relax (vide fig. 4). The rheobase was then determined by applying a long duration current (3 sec.) with instaneous rise. Subsequently, thresholds for currents

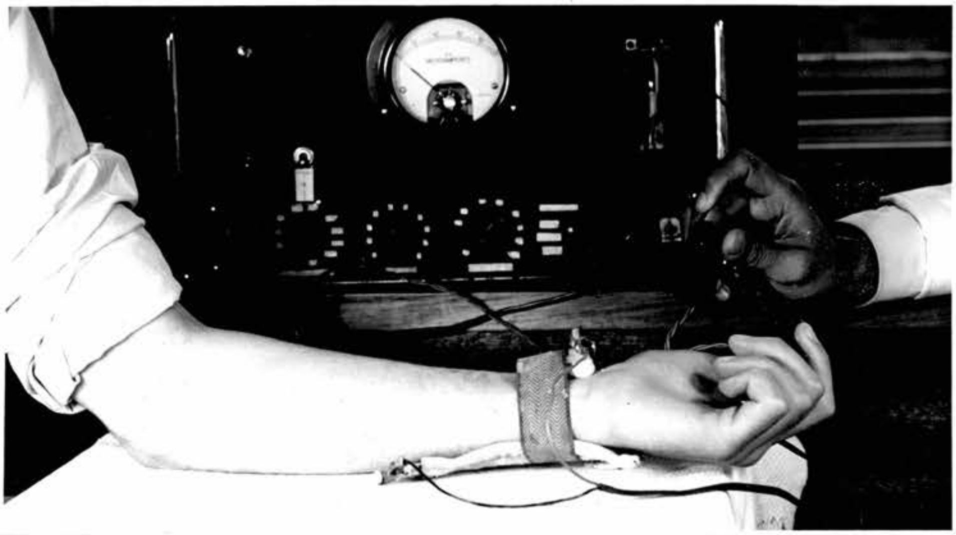


FIG.5

FIGURE 5

Shows the experimental set up for stimulating the median nerve at wrist (see text for details).

rising exponentially with time constants of 25, 50, 75, 100, 125, 175, 200, 225 and 250 milliseconds were determined. Minimal visible twitch of the first dorsal interosseous muscle was taken as the index of response to stimulation of the nerve. At the end of the procedure, the rheobase was re-determined. If the two measurements of the rheobase differed by more that 10% (Kugelberg, 1944) the whole procedure was repeated until the rheobases determined at the beginning and end of the experiment were within 10% of each other.

The same procedure was repeated with the cathode at the wrist over the anatomical site of the ulnar nerve and the anode in the neighbourhood. In the case of the median nerve, two sets of readings were obtained by stimulating the nerve with the cathode at the bicipital groove in front of the elbow and at the wrist with the cathode over the palmaris longus tendon (vide fig. 5). A minimal visible twitch of abductor pollicis brevis muscle was taken as the index of response to stimulation of the median nerve at both sites. The other details of the procedure were the same for the ulnar nerve.

<u>Set up for lateral popliteal nerve</u> : For the study of the lateral popliteal nerve, difficulty was encountered in stimulating the nerve with a surface

electrode over the neck of the fibula owing to the limited output of the stimulator. To overcome this, the nerve was stimulated with a hypodermic needle as cathode inserted through the skin in the neighbourhood of the nerve at the same site. The anode was placed on the medial surface of the tibia. The least visible upward movement of great toe was taken as the index of response to stimulation of the lateral popliteal nerve.

Frequency of application of stimuli :
Stimuli were applied at intervals exceeding 30 seconds to enable the nerve to recover its resting state between stimuli. The threshold for current pulses with each time constant was estimated by gradually increasing the current strengths on successive tests. It was found that this procedure gave consistent results whereas determination of the threshold by decreasing from suprathreshold levels gave variable results.

Suitability of the index used to determine threshold stimulation

In this work, visible muscle twitch has been used as index of response to nerve stimulation. Skoglund (1942) has deprecated the use of visible or palpable muscle contraction as an index of threshold stimulation in the study of accommodation. He observed that in determining the threshold strength for longer rising currents, it becomes difficult to visualise such a contraction. This is due to the repetitive discharges of nerve fibres resulting from breakdown of accommodation in response to sufficiently strong stimulating current. I have experienced similar difficulty with slowly rising currents, but the muscle contraction was observed to be a consistent index for obtaining the linear parts of the curves which have been used to measure the time constant of accommodation.

Kugelberg (1944) could obtain consistent results using muscle contraction as an index in his study which included a fairly large number of subjects.

In view of these facts, muscle contraction was considered a suitable index to determine a working accommodation curve in the peripheral motor nerves, although it may not be an ideal one. Moreover, adoption of this index permitted comparison of the results with those of Kugelberg (1944) which have been confirmed by Simpson (1955).

Skoglund (1942) has suggested that the actual accommodation in a nerve fibre could only be ascertained if the first nerve action potential recorded with the cathode ray oscilloscope is used as an index of stimulation of the fibre. Granit and Skoglund (1943) refined the method further by using a microelectrode for picking up the action potential from an isolated single fibre in animals.

A duplicate measurement of accommodation (by using appearance of first action potential as the index of stimulation) of a few subjects already studied by the method described was thought worthwhile for comparison. Accordingly, an attempt was made to record the action potential in a cathode ray oscilloscope with a needle electrode inserted into the relevant muscle. The method of stimulation remained the same as described before. Unfortunately, the stimulator used in the study could not be completely isolated from ground as the long-duration pulses of current cannot be transmitted through a transformer or radio frequency isolation unit. This failure of isolation resulted in production of a large stimulus artefact, which made recognition of action potentials impossible. Consequently this aspect of the work had to be abandoned.

Method of construction of accommodation curve

The stimulation threshold was plotted against the time constant of rise of the stimulating current in the manner of Solandt (1936). As the actual amount of current passing to the nerve depends on a number of factors such as tissue resistance, the absolute values for threshold currents are not of much significance by themselves. Thus the thresholds for the exponential currents were expressed in terms of their ratio to the rheobasic current, the latter being taken as unity. The accommodation curves were obtained by plotting on graph paper the relative current strengths as ordinate and the time constant of their rise as abscissa. In the rest of this thesis, the stimulating current will be specified by the time constant of its rate of rise, e.g. 'a 25 milliseconds pulse' indicates that the rising phase of the stimulus is exponential with a time constant of 25 milliseconds.

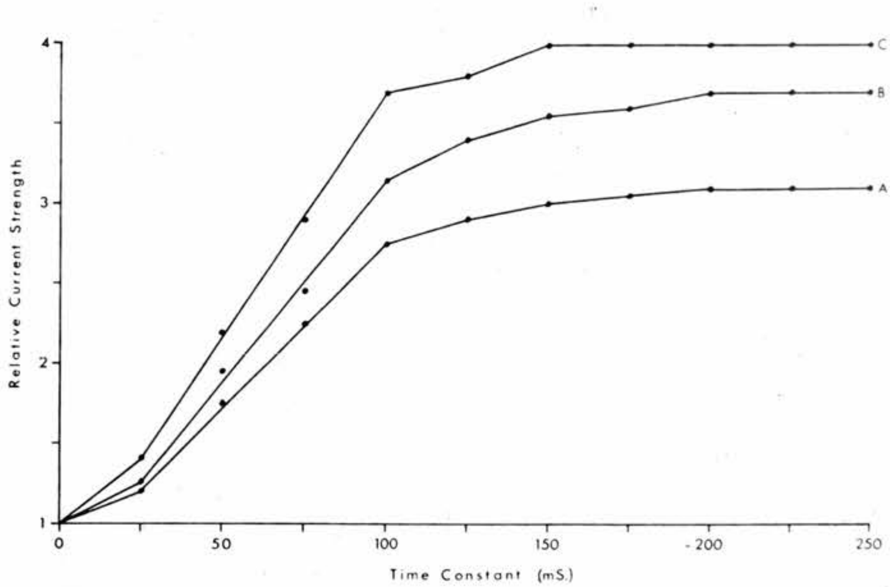
Measurement of accommodation

The accommodation slopes were computed by extrapolating the rectilinear part of the curve, and measured in multiples of rheobase per second (rheobase = 1) (Kugelberg, 1944). As the initial part of the curve often showed a deviation from linearity, for determination of the slope the beginning of the rectilinear part was taken at the point of the 25 milliseconds stimulus. Such initial deviation has also been reported by Solandt (1936). In a fair number of pathological curves, however, this initial bending was absent and on such occasions the beginning of the rectilinear part of the curve was taken at the point of 0 milli-seconds in the abscissa and the slope measured accordingly. The slope obtained by stimulating the ulnar or median nerve at elbow or wrist will be taken as the accommodation in the nerve at that site.

Breakdown of accommodation

Breakdown of accommodation was taken as the point where the rectilinear part of the curve took up a relatively horizontal course. This did not represent the actual point of breakdown of accommodation as the departure from linearity occured progressively, but it was considered to be suitable as an index for a comparative study between different groups of patients.

CHAPTER 3



Relative Current Strength
1
2
3
4
0
50
100
150
200
250
Time Constant (mS.)
A
B
C

FIG. 6

FIGURE 6

Shows the accommodation curves for the ulnar nerve at elbow (A), the median nerve at elbow (B) and the lateral popliteal nerve at neck of fibula (C) obtained in one of the control subjects (subject 1). The slopes measured 20.0, 25.2 and 30.0 rheobases per second respectively.

STUDIES ON CONTROL

Selection of subjects

Fifty-two control subjects were selected from the in-patients of the Neurological Unit, Northern General Hospital, Edinburgh. These patients had no clinical or laboratory evidence of peripheral nerve abnormality. It was assumed that the accommodation of their peripheral nerve would be within normal range.

Table 1. shows the distribution of the control subjects with respect to clinical diagnosis.

Nerves studied

In each, the accommodation curves for the motor fibres of the ulnar and the median nerves at the elbow and the wrist and for the lateral popliteal nerve at the neck of the fibula were plotted.

Results

Nature of the curves : The resultant accommodation curves were linear in the initial parts with a tendency to become horizontal later (vide fig. 6). This pattern was in conformity with the experience of the previous workers (vide chapter 1).

TABLE 1

CLINICAL DIAGNOSIS OF CONTROLS

Diagnosis	Number of patients
Disseminated Sclerosis	24
Cervical spondylosis	5
Myositis	1
Chorea	1
Facial Myoclonus	1
Thyrotoxicosis	2
Mental deficiency	1
Hysteria	1
Trigeminal neuropathy	1
Epilepsy	4
Friedreich's Ataxia	1
Parkinsonism	1
Syringomyelia	1
Devic's Disease	1
Neurosyphilis	1
No abnormality	6
Total patients	52

Accommodation slope values : The accommodation slope values for the motor fibres of the ulnar and the median nerves at different sites are shown in Table 2. The accommodation has been taken as the slope of the initial linear part and is expressed in terms of the rise of slope in rheobases per second. The group mean accommodation slopes of the control subjects were 21.3 ± 0.4 and 22.0 ± 0.5 rheobases per second for the ulnar nerve at elbow and at wrist respectively and 22.6 ± 0.6 and 22.0 ± 0.5 rheobases per second for the median nerve at elbow and at wrist respectively.

An analysis of the results showed that the values of accommodation slopes for the motor fibres obtained at elbow and at wrist were not significantly different from each other, both for the ulnar and for the median nerves (vide p.39). Accordingly the slope values for the motor fibres of respective nerves in individual subjects were calculated as the mean of the values at the elbow and at wrist. These values are presented in Table 3. The same Table also contains the accommodation slope measurements for the motor fibres of the lateral popliteal nerve.

Accommodation and the side of the body examined : The accommodation slope was measured for the motor

TABLE 2

ACCOMMODATION SLOPE IN RHEOBASES PER SECOND IN CONTROLS

Subject no.	Slope in Rheobases per second			
	Ulnar		Median	
	Elbow	Wrist	Elbow	Wrist
1.	20.0	22.0	25.2	29.3
2.	26.6	24.0	20.7	24.0
4.	18.0	17.0	20.0	18.0
5.	18.0	26.0	22.2	26.0
6.	22.0	20.0	23.1	22.0
8.	29.0	20.0	34.0	20.0
9.	18.0	24.0	22.0	18.6
10.	26.0	21.3	37.0	23.3
11.	20.0	16.0	20.0	24.0
12.	20.6	16.0	20.3	21.3
13.	26.0	22.0	20.0	20.0
14.	22.0	26.6	29.1	20.0
16.	17.3	16.3	22.0	20.0
17.	28.0	22.0	23.0	24.0
18.	18.0	20.0	21.0	24.6
19.	26.0	26.5	18.0	18.6
20. /				

Subject no.	Slope in Rheobases per second			
	Ulnar		Median	
	Elbow	Wrist	Elbow	Wrist
20.	23.3	23.0	20.0	17.3
21.	18.0	28.0	22.5	22.0
22.	23.3	16.6	20.0	16.0
24.	20.0	29.3	34.0	28.2
25.	18.0	22.6	25.0	25.0
26.	22.1	23.0	20.0	18.6
27.	20.0	20.0	20.0	22.0
28.	20.6	24.0	22.0	20.0
29.	20.0	20.0	20.0	22.0
30.	20.0	24.6	24.0	26.0
31.	19.0	22.0	16.3	26.0
32.	18.0	18.0	18.0	22.0
33.	20.6	23.3	22.0	24.0
34.	21.3	20.1	22.0	22.0
35.	23.3	18.0	19.3	19.0
36.	20.6	22.0	22.0	22.0
37.	24.0	26.0	22.0	28.0
38.	28.0	24.0	24.2	26.0
39.	20.2	23.3	21.0	23.0
40.	20.4	25.3	22.0	25.0
42.	18.0	22.0	20.0	22.0
43. /				

Subject no.	Slope in Rheobases per second			
	Ulnar		Median	
	Elbow	Wrist	Elbow	Wrist
43.	18.0	18.6	21.0	20.0
44.	18.0	18.0	19.0	18.0
45.	19.3	18.0	21.0	20.0
46.	18.0	18.0	19.3	19.0
47.	28.0	30.0	22.0	22.0
48.	20.0	23.0	27.0	25.0
49.	26.6	22.0	28.0	16.6
50.	18.0	18.0	20.0	16.6
51.	25.0	35.0	32.0	32.0
52.	21.2	23.3	24.6	20.6
53.	22.0	21.3	24.0	22.0
54.	21.3	21.3	24.0	22.0
55.	17.0	18.0	18.0	20.0
56.	19.3	18.0	18.0	18.0
57.	22.0	26.0	26.0	26.0
Mean	21.3 ±0.4	22.0 ±0.5	22.6 ±0.6	22.0 ±0.5
S.D.	3.0	4.0	4.4	3.7
Range	21.3 ±6.7	22.0 ±9.0	22.6 ±9.9	22.0 ±8.3

TABLE 3

ACCOMMODATION SLOPE IN RHEOBASES PER SECOND IN CONTROLS

Subject no.	Slope in rheobases per second		
	Ulnar	Median	Lat. Popliteal
1.	21.0	27.2	30.0
2.	25.3	22.3	36.4
4.	17.5	19.0	20.0
5.	22.0	24.1	30.0
6.	21.0	22.5	24.0
8.	24.5	27.0	23.4
9.	21.0	20.3	30.0
10.	23.6	30.1	36.0
11.	18.0	22.0	27.0
12.	18.3	20.8	25.0
13.	24.0	20.0	26.0
14.	24.3	24.5	32.0
16.	16.8	21.0	28.0
17.	25.0	23.5	34.0
18.	19.0	22.8	34.0
19.	26.2	18.3	28.0
20. /			

Subject no.	Slope in rheobases per second		
	Ulnar	Median	Lat. Popliteal
20.	23.1	18.6	30.0
21.	23.0	22.2	32.0
22.	19.9	18.0	25.0
24.	24.6	31.1	34.0
25.	20.3	25.0	32.0
26.	22.5	19.3	31.0
27.	20.0	21.0	24.0
28.	22.3	21.0	28.0
29.	20.0	21.0	27.8
30.	22.3	25.0	27.0
31.	20.5	21.1	32.0
32.	18.0	20.0	32.0
33.	21.9	23.0	26.6
34.	20.7	22.0	22.6
35.	20.6	19.1	25.3
36.	21.3	22.0	24.6
37.	25.0	25.0	30.0
38.	26.0	25.1	32.0
39.	21.7	22.0	30.0
40.	22.8	23.5	28.0
42.	20.0	21.0	26.0
43. /			

Subject no.	Slope in rheobases per second		
	Ulnar	Median	Lat. Popliteal
43.	18.3	20.5	24.0
44.	18.0	18.5	22.0
45.	18.6	20.5	24.0
46.	18.0	19.1	21.0
47.	29.0	22.0	32.0
48.	21.5	26.0	32.0
49.	24.3	22.3	32.0
50.	18.0	18.3	22.0
51.	30.0	32.0	26.6
52.	22.2	22.6	28.0
53.	21.6	23.0	27.0
54.	21.3	23.0	28.0
55.	17.5	19.0	20.0
56.	18.6	18.0	25.3
57.	24.0	26.0	32.0
Mean	21.6 ±0.4	22.3 ±0.5	28.0 ±0.6
S.D.	3.0	3.4	4.2
Range	21.6 ±6.7	22.3 ±7.6	28.0 ±9.4

fibres of the ulnar nerve at the elbow in both sides in 6 subjects of the control group to detect any possible difference between the capacities of accommodation in the same nerve of the two sides. The observed accommodation slopes are quoted in Table 4.

The mean difference between the two sides was 0.55 ± 0.88 rheobases per second. This degree of mean difference is not significant as the t of the same is 0.6 ($P > 0.2$) consequently it can be assumed that accommodation in the motor fibres of any particular nerve is similar in both sides. This observed similarity between the two sides points to the consistency of the method adopted in this study.

Discussion

Purposê of studying controls : The accommodation in the motor fibres in the peripheral nerves was measured in the controls for comparison with that of subjects with a definite peripheral nerve or anterior horn cell pathology. In addition, it was thought relevant to compare the present results with those of previous workers on normal human beings. Such a comparison was expected to throw some light on this scantily studied phenomenon in the peripheral nerves.

TABLE 4

ACCOMMODATION SLOPES FOR ULNAR NERVE AT ELBOW IN TWO LIMBS IN CONTROLS

Subject no.	Slope in rheobases per second	
	Right	Left
4.	18.0	20.0
8.	26.0	29.0
20.	23.0	23.3
24.	20.0	18.2
34.	21.3	19.1
46.	18.0	20.0

Comparison of available reports :

Ulnar nerve : The accommodation values of the ulnar nerve obtained by other workers for the motor fibres of the ulnar nerve are shown in Table 5., along with my own results.

The comparison shows that the accommodation slopes for the motor fibres of the ulnar nerve at elbow reported by different workers were closely similar, but not identical. The differences observed were possibly dependent upon the index used to determine the threshold of stimulation, the nature of the stimulator employed and possibly also on the actual experimental procedure. In the present study, every attempt was made to follow the method of Kugelberg as far as possible, and the accommodation slopes obtained by me (21.3 ± 0.4 rheobases per second) were not much different from those reported by Kugelberg (18.1 rheobases per second) (1944) using the same index.

A scrutiny of Kugelberg's (1944) results shows that the calculated slope may vary with the nature of the index of threshold stimulation used. He obtained a mean accommodation slope of 18.1 rheobases per second for the ulnar nerve at elbow, by using visible twitch of dorsal interosseous muscle as an index and means ranging between 21.4 and 23.0 rheobases

TABLE 5

MEAN ACCOMMODATION SLOPES FOR ULNAR NERVE AT ELBOW REPORTED BY DIFFERENT WORKERS

Author	Index of threshold stimulation	Number studied	Mean slope in rheo-bases per second
Solandt (1935-36)	Palpable twitch of flexor carpi ulnaris ms.	16	16.0
Skoglund (1942)	do	2	18.0
Kugelberg (1944)	do	100	21.4
	do	20	23.0
	do	15	22.0
	Visible twitch of adductor pollicis ms.	20	18.3
	Visible twitch of dorsal inter-osseous ms.	20	18.1
Author (1964)	do	52	21.3 ±0.4

per second for the same nerve at elbow by using palpable twitch of flexor carpi ulnaris as the index (vide Table 6).

Median nerve : Table 7 compares the mean accommodation slopes for the motor fibres of the median nerve by stimulation at elbow obtained in this study with those of Kugelberg (1944). As with the ulnar nerve, values reported by Kugelberg and those obtained by me are comparable; they were 19.5 and 22.6 ± 0.6 rheobases per second respectively. Kugelberg's values also show their dependence on the index used. He obtained a steeper curve (Slope = 25.6 rheobases per second), using palpable contraction of m. flexor carpi radialis as the index of stimulation than that with visible twitch of abductor pollicis brevis muscle as an index (Slope = 19.5 rheobases per second).

Comparison of the accommodation at different sites of the same nerve : A selective affection of the accommodation in peripheral nerves in tetany has been reported by Kugelberg (1944). Kugelberg and Skoglund (1946) observed a longer adaptation time in the proximal part than in the distal part of the same fibre of the ulnar nerve. The duration of the repetitive discharges in a single motor unit was taken as the measure of adaptation time. According to these workers, accommodation is inversely proportional to the adaptation. Hence,

TABLE 6

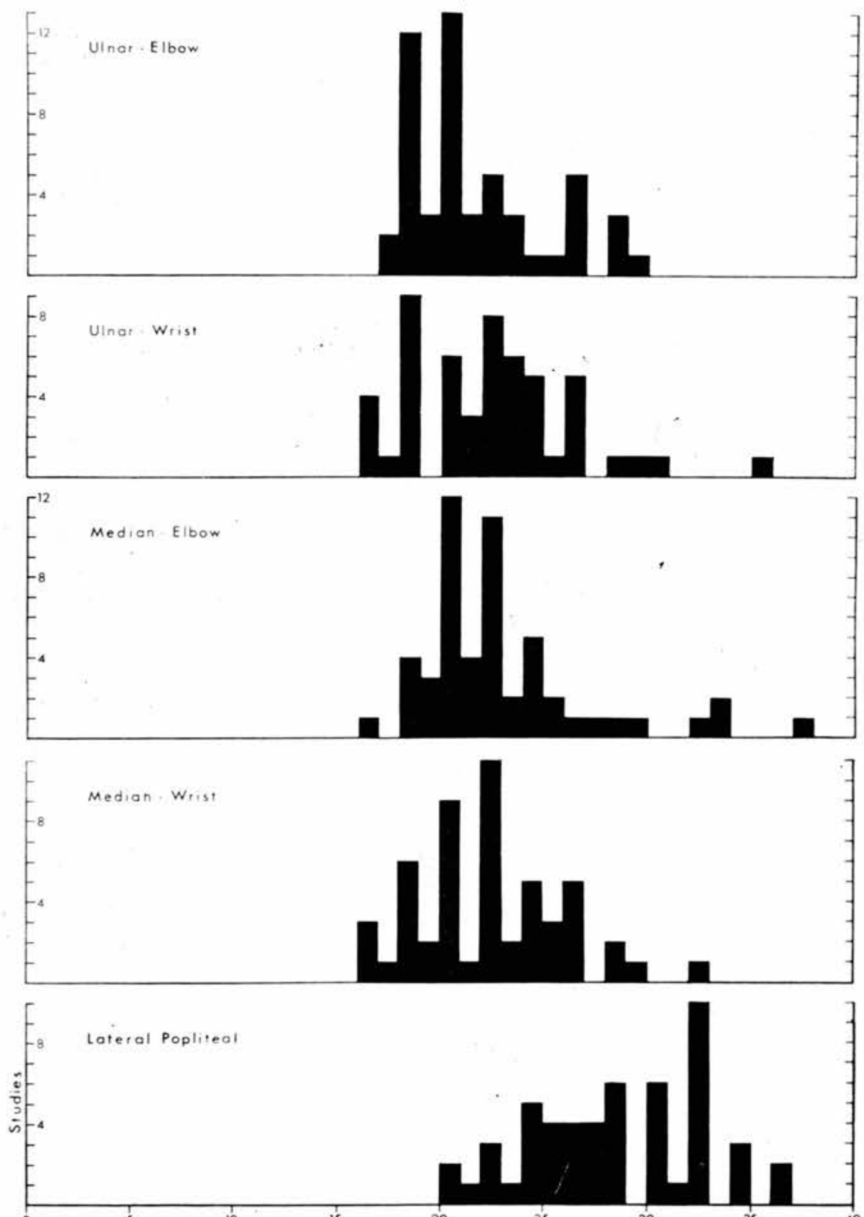
MEAN ACCOMMODATION SLOPES FOR ULNAR NERVE AT ELBOW WITH DIFFERENT INDICES OF THRESHOLD STIMULATION (Kugelberg, 1944)

Index of threshold of stimulation.	Mean slope in rheobases per second
Palpable contraction of flexor carpi ulnaris ms.	21.4 23.0 22.0
Visible twitch of 1st dorsal interosseous ms.	18.1

TABLE 7

COMPARISON OF MEAN ACCOMMODATION SLOPES FOR THE MEDIAN NERVE AT ELBOW OBSERVED BY KUGELBERG AND THE AUTHOR

Author	Index of threshold stimulation	Slope in rheobases per second
Kugelberg (1944)	Palpable contraction of flexor carpi radialis ms.	25.6
Kugelberg (1944)	Visible twitch of abductor pollicis brevis or opponens pollicis ms.	19.5
Present author (1964)	Visible contraction of abductor pollicis brevis ms.	22.6 ± 0.6



Ulnar - Elbow
Ulnar - Wrist
Median - Elbow
Median - Wrist
Lateral Popliteal
Studies
Rheobases per Second

FIG.7

FIGURE 7

Shows the distributions of the accommodation slope values for the different nerves among the controls.

they concluded that the proximal part of a nerve possesses less accommodation than the distal part. In the present study, no consistent relationship could be observed between the proximal and the distal parts of the ulnar nerve and the median nerve, sometimes the one and sometimes the other having the greater accommodation (vide Table 2.). The difference may well be in the fact that the most readily stimulated fibres at each site are unlikely to be the same. The distribution of the slope values of the motor fibres obtained at elbow and wrist were, however, almost similar for both the ulnar and median nerves (vide fig. 7.) and also the mean differences between the slope values of the two sites of the nerves were not significant. The data for the evaluation of the mean differences between the two sites are tabulated below (Table 8.).

TABLE 8.

Nerve	Mean difference	t	P
Ulnar	0.7 ± 0.5	1.2	>0.2
Median	0.6 ± 0.6	1.0	>0.2

Kugelberg (1944) also could not detect any difference in the accommodation for the motor fibres between the elbow and the wrist of the ulnar nerve using muscle twitch as the index of stimulation. This suggests that if there is a difference between the accommodation at wrist and at elbow in the same nerve fibre, it is too small to be detected by the present method in which a nerve bundle is stimulated. It is possible that a difference may be limited to the lowest threshold fibres. Kugelberg and Skoglund (1946) measured the threshold by the appearance of the first action potential using a micro-electrode; they obviously obtained the accommodation value for the lowest threshold fibres and were able to identify the stimulation of the nerve fibre at both sites. Their same study further shows that the accommodation measured by using action potential as an index was much smaller than that obtained by using muscle twitch as the index in the same subject. This suggests that lower threshold fibres may have a diminished capacity of accommodation. Sato (1950-51 b) however, observed a larger value of λ for smaller diameter fibres than the larger ones in his experiments with animals.

Comparison of accommodation between different nerves : Kugelberg (1944) on a comparative study of 15 subjects suggested that accommodation in the median nerve was somewhat better than in the ulnar nerve, but this observation of Kugelberg could not be confirmed in the present study, which has been carried out on a larger number of subjects. In the present study, 34 subjects (65.5%) among the controls had higher accommodation slope value in the motor fibres of the median nerve that those of the ulnar and 17 subjects (32.7%) had a lower value in the former than the latter. The mean difference of the values between the two nerves was not significant. The relevant data on the difference is shown below.

Mean difference	t	P
0.7 ± 0.4 rheobases per second	1.75	>0.05

The motor fibres of the lateral popliteal nerve, however were observed to have a higher degree of accommodation than those of the ulnar and the median nerves. A review of Table 3 will show that this difference was obtained in almost all the subjects of the control group. This fact is also obvious in fig. 7. The mean differences between the slope values for motor fibres of the lateral popliteal nerve and those of the ulnar and the median nerves are statistically significant (vide Table 9.).

Kugelberg on the contrary could not detect any difference in the accommodation of the nerves of the leg from those of the forearm in a study of 10 control subjects. He obtained a mean accommodation slope of 20.2 rheobases

TABLE 9

ANALYSIS OF THE MEAN DIFFERENCES BETWEEN LATERAL POPLITEAL NERVE AND MEDIAN AND ULNAR NERVES

Nerve	Mean difference (in rheobases per sec.)	t	P
Ulnar	6.4 ± 0.5	12	<0.001
Median	5.7 ± 0.3	19	<0.001

per second in the nerve of the leg. He used different indices to determine the threshold in different subjects in this group, accordingly the results obtained from such study is likely to be fallacious for reasons mentioned before (vide p.37).

Breakdown of accommodation : Breakdown of accommodation was found to occur at a current strength of 2 - 4 times the rheobase in the control subjects (vide fig. 6). This was in agreement with previous workers (Bernhard et al, 1942; Kugelberg, 1944).

Summary and conclusions

Accommodation was studied in 52 control subjects in the motor fibres of median and ulnar nerves at the elbow and wrist and in the lateral popliteal nerve at the neck of the fibula.

A comparison of the results obtained in the present study with those of the previous workers shows that the calculated value of accommodation depends on the experimental procedure. If the procedure is standardised, a comparable result can be obtained by the method used.

No difference could be observed in capacity of accommodation in the motor fibres between the ulnar and the median nerves, but faster accommodation (i.e. a lower time constant) was observed in the motor fibres of the lateral popliteal nerve than in those of the nerves of the forearm.

No regional difference in the capacity of accommodation along the length of a nerve could be detected by the method used.

A breakdown of accommodation occurred with any stimulus having a strength of 2 - 4 times that of the rheobase, regardless of its time constant of rise.

CHAPTER 4

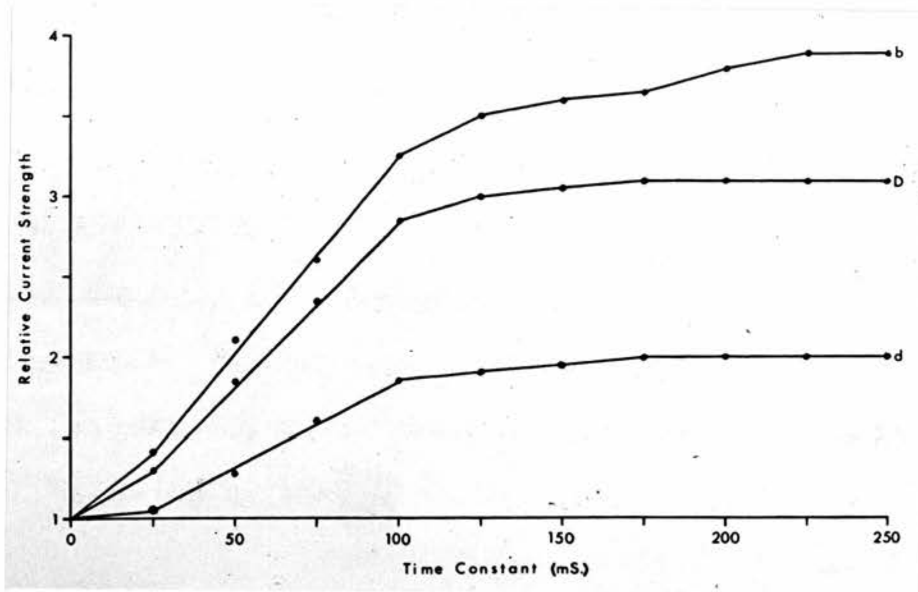
STUDIES ON COMPRESSION NEUROPATHY

Four subjects with compression neuropathy were studied in the present work. Three of them were patients with compression of the median nerve between the carpus and the flexor retinaculum of the wrist (Carpal tunnel syndrome) and the other was a patient suffering from pressure palsy of the ulnar nerve at the elbow.

Carpal tunnel syndrome

Diagnosis : The diagnosis in these three subjects was established on the following criteria :

1. Presence of a spontaneous sensation of 'pins and needles' in the thumb, index and middle fingers of one or both hands.
2. Some wasting of the lateral part of the thenar eminence.
3. Weakness of one or more muscles of the thenar eminence supplied by the median nerve.
4. Absence of any evidence of a lesion of any other peripheral nerve.
5. Slowing of conduction along the median nerve at the carpal tunnel detected by measuring the conduction velocity of the nerve proximal and distal



Relative Current Strength
Time Constant (mS.)
4
3
2
1
0
50
100
150
200
250
b
D
d

FIG.8

FIGURE 8

Shows the accommodation curves for the median nerve at elbow (b) and at wrist (d) obtained in a patient with carpal tunnel syndrome (Case no. 8106). A curve for the median nerve at wrist from a control subject is also shown for comparison(D). Slope values : (b) = 24.2, (d) = 10.0 and (D) = 20.0 rheobases per second.

5. to the flexor retinaculum (Simpson, 1956).

Nerves studied : The accommodation curve was drawn and the values of the slopes were calculated by the method described for the median and ulnar nerves at the wrist and in the median nerve at the elbow in these patients. The accommodation was measured in both sides.

Results

Nature of curves : Figure 8 shows the accommodation curves for the motor fibres of the median nerve at elbow and at wrist obtained in one of the patients with a carpal tunnel syndrome. The curve for the elbow is not different from a normal curve (vide fig. 6.). The curve for the wrist, however, differs in many aspects from a normal one (vide fig. 8). The curve is less steep than the normal curves for the wrist. The 'breakdown' of accommodation has occurred at a lower current strength (1.85 rheobases) than normal (2 - 4 rheobases). All the curves for the wrist in patients with carpal tunnel syndrome conformed to this pattern.

Accommodation slope values : Table 10, containing the results obtained in those patients shows that the values of the accommodation slopes in the motor fibres of the median nerve were lower at the wrist than at the elbow. The mean difference between the two sites were 11.8 ± 1.25 rheobases per second for the right nerve and

TABLE 10

ACCOMMODATION SLOPES IN MEDIAN NERVE AT ELBOW AND AT WRIST IN CASES OF CARPAL TUNNEL SYNDROME

Case No.	Name	Slope in rheobases per second			
		Right side		Left side	
		Elbow	Wrist	Elbow	Wrist
6981	E.M.	20.0	10.0	22.0	16.0
8106	E.O.	24.2	10.0	21.6	12.0
8107	S.H.	23.2	12.0	23.0	16.0

7.5 ± 1.1 rheobases per second for the left. The relevant data for the analysis of the difference are shown in the Table below.

Side	Mean difference	t	P
Right	11.8 ± 1.25	9.0	<0.02
Left	7.5 ± 1.1	6.8	<0.05

It has been shown in Chapter 3 that there is no significant difference of accommodation along the length of the median nerve normally, so this reduction in accommodation in the fibres of the median nerve at wrist in patients with carpal tunnel syndrome can be accepted as abnormal. The limitation of this reduction to the site of the compression is indicated by the fact that the slopes for the median nerve at elbow were within the normal range (22.6 ± 9.9 rheobases per second = control range). This abnormality of the median nerve at wrist is emphasised by comparing the group mean accommodation of these patients with that of controls. The comparative data are shown in Table 11.

The impaired accommodation at the wrist in the motor fibres of the median nerve in patients with carpal tunnel syndrome is also substantiated by inspection of individual results. Among the six measurements of accommodation

TABLE 11

COMPARISON OF GROUP MEAN ACCOMMODATION SLOPES FOR MEDIAN NERVE AT WRIST IN CONTROLS AND IN PATIENTS WITH CARPAL TUNNEL SYNDROME

Mean slope in rheobases per second			t	P	f
Control	Carpal tunnel syndrome				
22.0 ± 0.5	Right	10.6 ± 0.9	5.0	<0.001	53
	Left	14.6 ± 1.5	3.3	<0.01	53

slope for the motor fibres of the median nerve at the wrist in these patients, four (66%) had a slope value of 12 rheobases per second or less and two (33%) had a slope value of 16 rheobases per second. Analysing the distribution of the slope values in controls, it was calculated that among the normal population only 0.7% and 10.8% had probabilities of having slope values as low as 12 rheobases per second and 16 rheobases per second respectively for these fibres.

Accommodation in the motor fibres of the ulnar nerve at the wrist in these patients was found to be within the range of the controls; this finding excluded the possibility of any generalised impairment of accommodation in the peripheral part of the motor fibres.

In one of these patients (Case no 6981), the study was repeated about a year after operative splitting of the flexor retinacula of both sides to decompress the median nerve. The patient had considerable symptomatic improvement after the operation. The slopes obtained in this patient after the operation along with the pre-operative values are shown in Table 12.

From the figures shown in Table 12 there is some suggestion that the accommodation in the motor fibres of the right median nerve has returned towards the

TABLE 12

THE EFFECT OF DECOMPRESSION ON THE ABNORMAL ACCOMMODATION IN CARPAL TUNNEL SYNDROME

	Slope in rheobases per second			
Side	Elbow		Wrist	
	Before oprn.	After oprn.	Before oprn.	After oprn.
Right	24.6	20.0	10.0	16.5
Left	—	—	16.0	14.0

normal range, but as no similar change occured on the left, it is impossible to draw any general conclusion.

Ulnar nerve compression

As mentioned before, the other subject in the group of compression neuropathy was a patient suffering from pressure palsy of the ulnar nerve at the elbow. A short summary of the case history is noted below.

Case history : J.H., aged 37, attended the neurological out-patient clinic complaining of numbness of right little finger, the medial half of ring finger and the corresponding part of the distal third of the forearm. He was also having feelings of pins and needles in this area from time to time. On examination, hypoaesthesia and hypoalgesia were noted in that area. There was slight weakness of the hypothenar muscles of the right side. Nerve conduction study revealed a slowing of conduction along the right ulnar nerve at the elbow. Although he denied any history of compression, in absence of any other reason to explain such a localised lesion at this site, a diagnosis of compression of ulnar nerve at elbow was made.

<u>Nerves studied</u> : The accommodation slopes for the motor fibres of both ulnar nerves were computated at the wrist and at the olecranon groove of the elbow by the usual method.

<u>Results</u> : All the slopes were within the normal range with the exception of that measured at the right elbow, the presumed site of compression of the right ulnar nerve (vide Table 13.) which was lower than the value of the control range (21.3 ± 6.7 rheobases per second = control range for ulnar nerve at elbow).

Discussion

The results described above have been obtained from a small group of subjects with compression neuropathies since no more cases were available for study. Any inference drawn from these results must therefore be a tentative one requiring confirmation in a larger series.

Despite the limitations imposed by the small number of subjects, a statistically significant reduction of the accommodation in the motor fibres at the site of compression both in patients with carpal tunnel syndrome and in the patient with ulnar palsy suggests that there is a localised impairment of accommodation

TABLE 13

ACCOMMODATION SLOPE FOR ULNAR NERVE AT ELBOW AND AT WRIST IN PRESSURE PALSY OF ULNAR NERVE

Case No.	Name	Side	Slope in rheobases per second	
			Elbow	Wrist
7857	J.H.	Right	11.3	20.0
		Left	20.0	19.3

at the site of compression of a peripheral nerve. A selective alteration of accommodation in one part of a nerve leaving the other parts unaffected has been reported by Kugelberg (1944).

The pathogenesis of compression neuropathy has been thought similar to tourniquet paralysis (Simpson, 1956). In acute experiments, application of a tourniquet has been found to affect the accommodation of the peripheral nerve concerned (Kugelberg, 1944). In such experiments, the accommodation was found to be impaired immediately after the compression, becoming raised on continuation of compression. Release of the compression led to transient subnormality of accommodation again. The effect of chronic compression of a nerve on its accommodation has not been reported previously.

. The present study shows that in chronic compression an impairment of accommodation of motor nerve fibres may occur at the site of compression and suggests that this may be irreversible (vide Table 12.).

Though the accommodation of the sensory fibres was not studied, it is likely that this is also impaired in compression neuropathy. Impairment of accommodation in the sensory fibres is considered to produce paraesthesia in the distribution of the affected nerve (Kugelberg, 1944) and the paraesthesia in the fingers which is a prominent feature of the carpal tunnel syndrome may be a manifestation of such impairment. This may also explain the exacerbation of ischaemic paraesthesia (Gilliat & Wilson, 1953) observed in these subjects; ischaemia worsening the impaired accommodation further.

The possibility of an impairment of accommodation in compression neuropathy was suggested by Simpson (1956). He based his suggestion on his detection of repetitive responses in the thenar muscles in response to a single stimulus to the median nerve at the wrist in patients with carpal tunnel syndrome and in the hypothenar muscles in compression neuropathy of the ulnar nerve.

Threshold stimulation of normal nerve fibres does not usually cause iterative firing. This is mainly attributed to the accommodation property of a peripheral nerve. Repetitive responses have been noted in nerve fibres where there is an impairment of accommodation e.g. in hypocalcaemic subjects (Katz, 1937), in nerves of cooled frogs and nerves bathed in calcium free fluid. Normal crabs' and lobsters' nerves which have little or no accommodative property have also been observed to behave in the same manner (Hodgkin, 1948).

It must be mentioned, however, that accommodation, though an important one, is not the only factor which controls the "repetitiousness" in a nerve (Katz, 1937). Sato (1950-51a) in his study on the effects of hypertonic saline on nerve excitability, failed to correlate the incidence of repetitive responses with impaired accommodation and concluded that retardation of the recovery process is responsible for repetitive responses to near threshold current.

An observation in one of the subjects of the present author suggests the possibility of other factors than accommodation also playing a role in the production of repetitive responses in a nerve fibre. Accommodation was studied in the ulnar nerve of a subject showing a repetitive response in the hypothenar muscles in response to a single stimulus to the ulnar nerve. He had no other objective evidence of a neurological disorder. Accommodation of the ulnar nerve was found to be within the normal range both at the elbow and at the wrist. The values of the accommodation slopes were 22.2 and 24 rheobases per second respectively. It may be that the iterative responses seen during conductivity studies were confined to a few motor fibres which were not stimulated in my studies, but the possibility of other factors than accommodation being responsible for repetitive firing in certain circumstances must be borne in mind.

Summary and conclusions

Accommodation was studied in the motor fibres of the nerves of the upper limbs in four patients with compression neuropathy.

The results show that compression of a peripheral nerve may lead to an impairment of accommodation at the site of compression. There is a further suggestion that this impairment may be irreversible in some cases.

The study suggests that repetitive responses observed to stimulation of the affected nerve in compression neuropathy are likely to be due to the lowered accommodation of the nerve at the site of compression.

There is also support for the contention that the presence of repetitive responses in a nerve does not necessarily indicate impairment of accommodation in the corresponding nerve.

CHAPTER 5

STUDIES ON POLYNEUROPATHY

Definition of the term polyneuropathy

In this study, the term has been used to indicate a pathological condition with clinical evidence of impairment of function of many peripheral nerves simultaneously and usually symmetrically. Compression neuropathy was not included in this group.

Subjects studied

The subjects with polyneuropathy comprising this series could be divided into the following groups :

1. Pure sensory polyneuropathy : This group was comprised of those patients who complained of a sensation of 'pins and needles' bilaterally in upper and / or lower extremities, with or without loss of sensation to pinprick and / or touch in those areas. Deep reflexes were normal or diminished, but none had any obvious muscle weakness or wasting. No retardation of conduction in the motor fibres was detected in any of them.
2. Pure motor polyneuropathy : Subjects having weakness in the limbs of peripheral nerve distribution with loss of deep reflexes of the corresponding parts with or without muscle wasting and with

no subjective or objective sensory symptoms were grouped under this heading. Conduction velocity was retarded in motor fibres of peripheral nerves in most of them.

3. Sensory-motor ('mixed') polyneuropathy : Subjects included in this group had combined features of motor and sensory neuropathy.

4. Vitamin B_{12} deficiency polyneuropathy : In the patients with peripheral neuropathy due to Vitamin B_{12} deficiency, it was not always possible to determine the involvement of motor fibres of the peripheral nerves clinically due to presence of associated lateral column involvement. These subjects accordingly have been considered in a different group for the study.

In Table 14, the number of patients belonging to the different groups of polyneuropathy studied in the present work is shown.

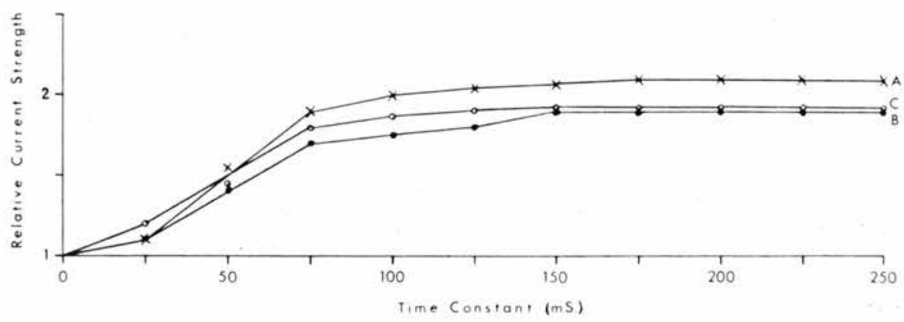
Nerves studied

The median and ulnar nerves were studied at elbow and at wrist and the lateral popliteal nerve at neck of fibula in each case. The study was carried out on both sides. The methods of study and of computation of

TABLE 14

PATIENTS IN GROUPS OF POLYNEUROPATHY

Group of polyneuropathy	Number of Patients
Sensory	7
Motor	6
Sensory-motor	3
Vitamin B_{12} deficiency	3
Total	19



Relative Current Strength
2
1
0
50
100
150
200
250
Time Constant (mS.)
A
C
B

FIG.9

FIGURE 9

Shows the accommodation curves for the ulnar (A) and the median (B) nerves at elbow and the lateral popliteal nerve at neck of fibula (C) in a patient with polyneuropathy involving motor fibres (Case no. 7554 in Table 16). Slope values : (A) = 16, (B) = 12, (C) - 12 rheobases per second.

accommodation slopes were the same as for the controls.

Results

Nature of the accommodation curves : In patients with sensory polyneuropathy, the accommodation curves obtained for the motor fibres of the different nerves were similar to those of the controls.

The nerves (motor fibres) of the patients with motor, sensory - motor and vitamin B_{12} deficiency polyneuropathies on the other hand, had curves differing significantly from the normal curves (three such abnormal curves have been reproduced in figure 9 from a patient with 'mixed' neuropathy). The initial linearity of the normal curves was maintained in these curves but in most, the slope of the initial linear part was flatter than normal. The deviation from linearity at the 25 millisecond point was lacking in many of these abnormal curves.

'Breakdown' of accommodation was observed with a smaller current strength than normal in the nerves (motor fibres) with flatter accommodation slope. This feature of 'early breakdown' was evident even in nerves having curves with a normal slope.

Accommodation slope values : The values of the slopes of the accommodation curves for the motor fibres obtained in individual subjects of the different groups of polyneuropathyes are shown in Tables 15, 16 and 17. It may be mentioned that in disease the same nerve of the two sides may not be affected to the same degree, hence the accommodation slope values obtained for a nerve on either side have been shown as separate observations. For the same reason, the group mean accommodation slope value for any particular nerve has been expressed separately for the right and left sides.

<u>Comparison between the accommodation slope values for the patients with polyneuropathy and for the controls</u> : The tables 18. 19 and 20 compare the mean values of accommodation slopes for the peripheral nerves (motor fibres) of the different groups of polyneuropathies with those of the controls. In normal persons, no difference exists in the accommodation of a nerve between the two limbs, so it was thought permissible to compare the same group mean accommodation slope value for a nerve of the controls with the group mean accommodation slope value for the same nerve of either side of the patients with neuropathy.

<u>Sensory group</u> : It is seen from Table 18 that there was no significant difference between the mean values for the nerve of the patients with sensory neuropathy and those of the controls so far as motor fibres were concerned. The <u>t</u> of the difference of the group

TABLE 15

ACCOMMODATION SLOPES FOR MOTOR FIBRES IN SENSORY POLYNEUROPATHY

Case No.	Name	Side	Slope in rheobases per second				
			Ulnar		Median		Lat. Pop.
			Elbow	Wrist	Elbow	Wrist	
6896	T.H.	Right	22.0	19.0	20.0	24.0	31.0
		Left	24.0	21.0	24.0	22.2	24.0
6775	E.L.	Right	22.0	21.0	20.0	21.0	26.0
		Left	21.5	23.2	19.2	22.5	22.4
6700	M.S.	Right	19.0	18.0	21.0	20.0	26.0
		Left	19.5	19.5	23.0	20.8	30.0
7381	C.P.	Right	14.0	13.0	14.0	16.0	27.3
		Left	16.2	17.5	18.0	18.0	28.0
8168	E.B.	Right	23.0	23.3	25.0	22.0	31.0
		Left	22.0	23.0	22.7	21.0	28.2
7104	M.S.	Right	26.0	24.0	24.0	23.0	18.0
		Left	24.0	21.0	25.0	21.4	16.5

TABLE 16

ACCOMMODATION SLOPES FOR MOTOR FIBRES IN MOTOR AND 'MIXED' POLYNEUROPATHIES

Case No.	Name	Side	Slope in rheobases per second				
			Ulnar		Median		Lat.Pop.
			Elbow	Wrist	Elbow	Wrist	
7017	M.Mc.	Right	22.0	20.0	24.0	18.0	18.3
		Left	20.0	19.8	24.2	17.2	22.3
7070	T.F.	Right	22.0	18.0	20.0	18.0	Measured
		Left	20.2	19.2	18.2	18.4	on 19.3.63
7070	T.F.	Right	10.0	6.0	12.0	6.0	Measured
		Left	9.0	6.4	10.5	7.5	on 12.1.64
6377	C.H.	Right	18.0	14.0	10.0	5.0	18.0
		Left	16.0	12.8	9.5	13.0	16.2
6558	J.P.	Right	10.0	8.0	9.1	12.0	21.5
		Left	12.8	8.2	6.7	15.0	24.0
7789	I.B.	Right	20.0	22.1	20.5	20.0	21.3
7233 /		Left	21.2	21.3	19.5	18.0	20.1

Case No.	Name	Side	Slope in rheobases per second				
			Ulnar		Median		Lat.Pop.
			Elbow	Wrist	Elbow	Wrist	
7233	E.C.	Right	13.3	13.3	12.5	13.2	18.1
		Left	13.1	12.0	11.8	10.8	17.5
7554	G.C.	Right	16.0	7.5	12.0	5.0	12.0
		Left	14.0	8.3	13.5	6.8	13.2
7042	M.M.	Right	7.5	6.6	8.2	5.2	17.3
		Left	9.4	5.2	7.5	4.4	18.2
8015	J.M.	Right	18.0	15.0	19.0	14.1	10.3
		Left	16.0	14.2	17.0	13.1	14.0
7916	A.P.	Right	18.0	19.2	20.2	16.0	20.0
		Left	20.2	18.5	20.6	15.5	28.3

TABLE 17

ACCOMMODATION SLOPES FOR MOTOR FIBRES IN VITAMIN B_{12} DEFICIENCY POLYNEUROPATHY

Case No.	Name	Side	Slope in rheobases per second				
			Ulnar		Median		Lat. Pop.
			Elbow	Wrist	Elbow	Wrist	
6161	R.D.	Right	16.2	17.5	14.2	13.7	13.2
		Left	14.5	15.7	15.5	15.1	12.0
7133	J.C.	Right	11.3	10.2	11.8	11.2	18.4
		Left	12.2	12.8	12.2	10.2	16.2
7899	J.H.	Right	16.4	14.5	13.4	12.8	16.2
		Left	16.6	15.6	12.4	13.2	15.4

TABLE 18

COMPARISON OF GROUP MEAN ACCOMMODATION SLOPES FOR MOTOR FIBRES IN SENSORY POLYNEUROPATHY AND IN CONTROLS

Nerve	Slope in rheobases per second Control		Neuropathy	t	P	f
Ulnar (Elbow)	21.3 ± 0.4	Right	21.0 ± 1.7	0.2	>0.9	56
		Left	21.2 ± 1.2	0.07	>0.9	56
Ulnar (Wrist)	22.0 ± 0.5	Right	19.7 ± 1.6	1.2	>0.1	56
		Left	20.9 ± 0.8	1.2	>0.1	56
Median (Elbow)	22.6 ± 0.6	Right	20.7 ± 1.5	1.4	>0.1	56
		Left	22.0 ± 1.5	0.4	>0.5	56
Median (Wrist)	22.0 ± 0.5	Right	21.0 ± 1.0	0.6	>0.5	56
		Left	21.0 ± 0.5	0.6	>0.5	56
Lateral Popliteal	28.0 ± 0.6	Right	26.6 ± 1.9	0.7	>0.4	56
		Left	24.8 ± 2.0	1.7	>0.5	56

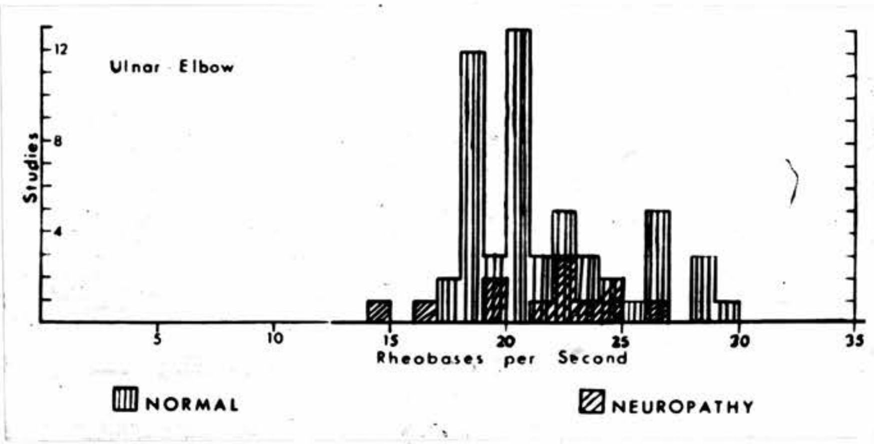

Ulnar Elbow
Studies
12
8
4
5
10
15
20
25
30
35
Rheobases per Second
NORMAL
NEUROPATHY

FIG.10

FIGURE 10

Shows the distributions of the accommodation slope values for the ulnar nerve at elbow among the patients with sensory neuropathy and among the normals (controls).

means between the two had a value of P greater than 0.05.

The distribution of accommodation slope values for the motor fibres of the ulnar nerve at elbow in the patients with sensory polyneuropathy has been compared with that in the normals (controls) in a histogram (vide figure 10). This comparison shows a similarity of the distributions in these two groups. The individual slope values for the motor fibres of the other peripheral nerves in the patients of this group of polyneuropathy were also within the respective normal (control) ranges. This would be evident from a perusal of Table 15.

Other groups : Table 19 shows a significantly lower group mean accommodation slope in the motor fibres of the patients with motor and 'mixed' polyneuropathies. This lowering was observed in all the nerves studied. A similar significant lowering was found in the motor fibres of the patients with vitamin B_{12} deficiency polyneuropathy (vide Table 20.).

The distribution of the accommodation slope values obtained in the motor fibres of the different nerves of the patients with motor, 'mixed' and vitamin B_{12} deficiency polyneuropathies is compared with that in the normals (controls) in a histogram (vide figure 11.). The comparison shows a 'shift to the left' (i.e. relatively more observations of smaller values) in the patients

TABLE 19

COMPARISON OF MEAN ACCOMMODATION SLOPES FOR MOTOR FIBRES IN POLYNEUROPATHIES WITH MOTOR INVOLVEMENT

(i.e. those belonging to the group of motor and mixed neuropathies), AND CONTROLS

Nerve	Slope in rhoebases per second Control		Neuropathy	t	P	f
Ulnar (Elbow)	21.3 ± 0.4	Right	15.9 ± 1.5	4.8	< 0.001	61
		Left	15.6 ± 1.3	5.0	< 0.001	61
Ulnar (Wrist)	22.0 ± 0.5	Right	13.6 ± 1.7	6.0	< 0.001	61
		Left	13.2 ± 1.7	6.0	< 0.001	61
Median (Elbow)	22.6 ± 0.6	Right	15.2 ± 1.6	5.0	< 0.001	61
		Left	14.4 ± 1.7	5.0	< 0.001	61
Median (Wrist)	22.0 ± 0.5	Right	12.0 ± 1.7	7.0	< 0.001	61
		Left	12.7 ± 1.5	7.0	< 0.001	61
Lateral Popliteal	28.0 ± 0.6	Right	17.4 ± 1.3	7.0	< 0.001	59
		Left	19.3 ± 1.5	5.0	< 0.001	59

TABLE 20

COMPARISON OF MEAN ACCOMMODATION SLOPES FOR MOTOR FIBRES IN VITAMIN B DEFICIENCY POLYNEUROPATHY AND IN CONTROLS

Nerve	Slope in rheobases per second: Control		Neuropathy	t	P	f
Ulnar (Elbow)	21.3 ± 0.4	Right	14.6 ± 1.7	3.0	<0.01	53
		Left	14.4 ± 1.4	4.0	<0.001	53
Ulnar (Wrist)	22.0 ± 0.5	Right	14.1 ± 2.0	3.0	<0.01	53
		Left	14.7 ± 1.6	3.0	<0.01	53
Median (Elbow)	22.6 ± 0.6	Right	13.1 ± 0.7	3.0	<0.01	53
		Left	13.3 ± 1.5	3.0	<0.01	53
Median (Wrist)	22.0 ± 0.5	Right	12.5 ± 1.0	4.0	<0.001	53
		Left	12.8 ± 1.5	4.0	<0.001	53
Lateral Popliteal	28.0 ± 0.6	Right	15.9 ± 1.7	5.0	<0.001	53
		Left	14.5 ± 1.4	5.0	<0.001	53

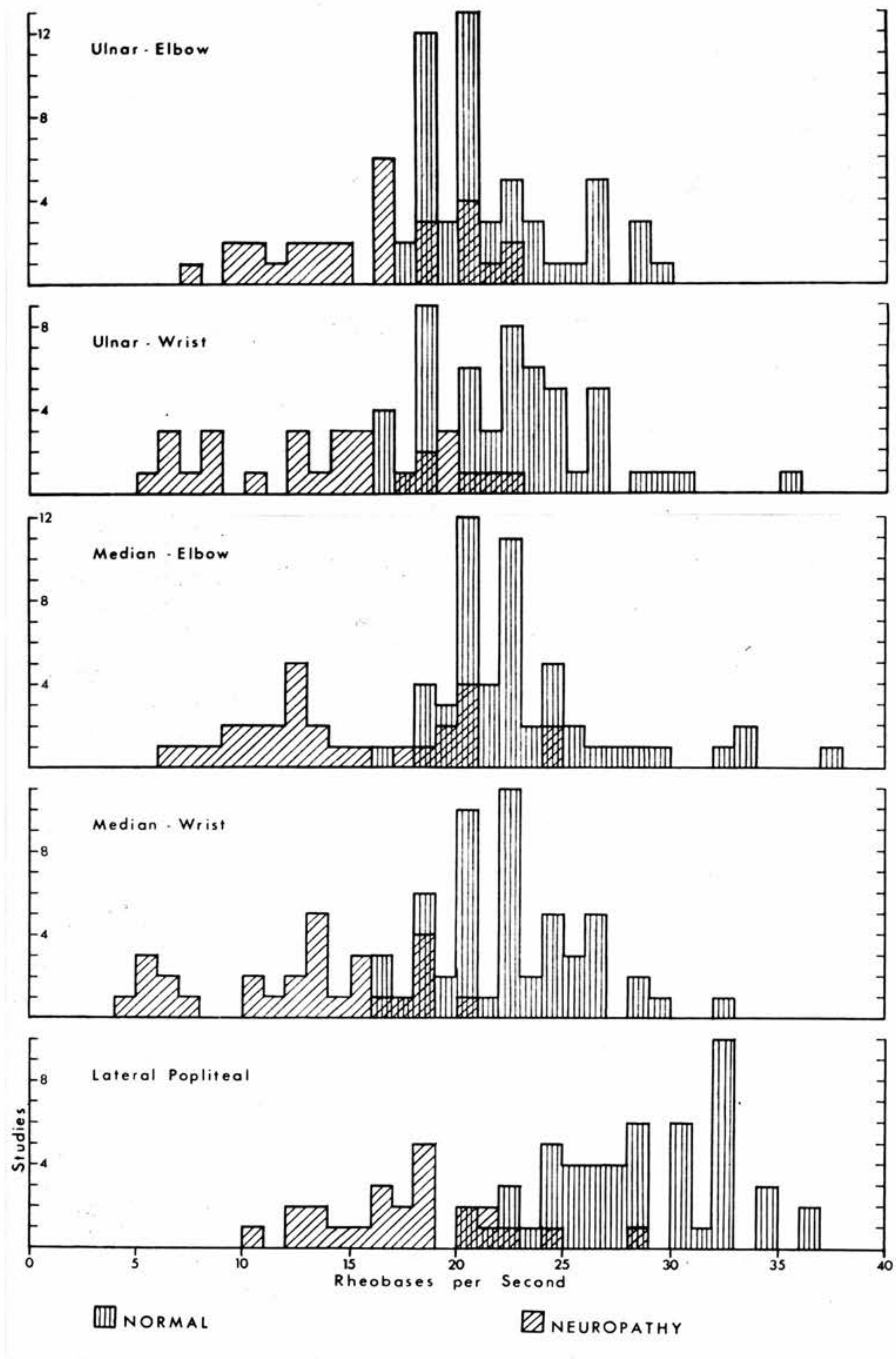

Ulnar - Elbow
Ulnar - Wrist
Median - Elbow
Median - Wrist
Lateral Popliteal
Studies
Rheobases per Second
NORMAL
NEUROPATHY

FIG. 11

FIGURE 11

Shows the distributions of the accommodation slope values for the different nerves among the patients with polyneuropathy (motor, 'mixed' and vitamin B_{12} deficiency) and among the normals (controls).

with neuropathy.

Attempts have been made to correlate the values of the accommodation obtained in the polyneuropathy subjects with other clinical features.

Correlation of accommodation with the degree of muscle weakness : I have not made a detailed study of the relationship between accommodation failure in motor fibres and the degree of weakness, but a few observations suggest that there is no close relationship between the two.

Relationship of impaired accommodation with muscle wasting : The patients belonging to the groups with impaired accommodation could be divided into those with more than moderate wasting of the muscles of the hands and forearms and those with minimal or no wasting of these parts. In Tables 21 and 22, the values of accommodation slopes in the motor fibres obtained in individual subjects of these two groups are shown.

The distribution of the slope values for the motor fibres of the nerves in the patients of those two groups has been compared in a histogram (vide figure 12). This figure shows the preponderance of relatively smaller slope values among the patients with muscle wasting than among those without any wasting. It emphasises the relatively greater impairment of accommodation in the motor fibres

TABLE 21

ACCOMMODATION SLOPES FOR THE MOTOR FIBRES IN POLYNEUROPATHY WITH MINIMAL OR NO MUSCLE WASTING

Case no.	Name	Side	Slope in rheobases per second			
			Ulnar		Median	
			Elbow	Wrist	Elbow	Wrist
6161	R.D.	Right	16.2	17.5	14.2	13.7
		Left	14.5	15.7	15.5	15.1
7133	J.C.	Right	11.3	10.2	11.8	11.2
		Left	12.2	12.8	12.2	10.2
7899	J.H.	Right	16.4	14.5	13.4	12.8
		Left	16.6	15.6	12.4	13.2
7017	M.Mc.	Right	22.0	20.0	24.0	18.0
		Left	20.0	19.8	24.2	17.2
7070	T.F.	Right	22.0	18.0	20.0	18.0
		Left	20.2	19.2	18.2	18.4
6558	J.P.	Right	10.0	8.0	9.1	12.0
		Left	12.8	8.2	6.7	15.0
7789 /						

Case no.	Name	Side	Slope in rheobases per second			
			Ulnar		Median	
			Elbow	Wrist	Elbow	Wrist
7789	I.B.	Right	20.0	22.1	20.5	20.0
		Left	21.2	21.3	19.5	18.0
7233	E.C.	Right	13.3	13.3	12.5	13.2
		Left	13.1	12.0	11.8	10.8
7916	A.P.	Right	18.0	19.2	20.2	16.0
		Left	20.2	18.5	20.6	15.5
8015	J.M.	Right	18.0	15.0	19.0	14.1
		Left	16.0	14.2	17.0	13.1

TABLE 22

ACCOMMODATION SLOPES FOR MOTOR FIBRES IN POLYNEUROPATHY WITH MORE THAN MINIMAL MUSCLE WASTING

Case no.	Name	Side	Slope in rhoobases per second			
			Ulnar		Median	
			Elbow	Wrist	Elbow	Wrist
7554	C.C.	Right	16.0	7.5	12.0	5.0
		Left	14.0	8.3	13.5	6.8
7042	M.M.	Right	7.5	6.6	8.2	5.2
		Left	9.4	5.2	7.5	4.4
7070	T.F.	Right	10.0	6.0	12.0	6.0
		Left	9.0	6.4	10.5	7.5
6377	C.H.	Right	18.0	14.0	10.0	5.0
		Left	16.0	12.8	9.5	13.0

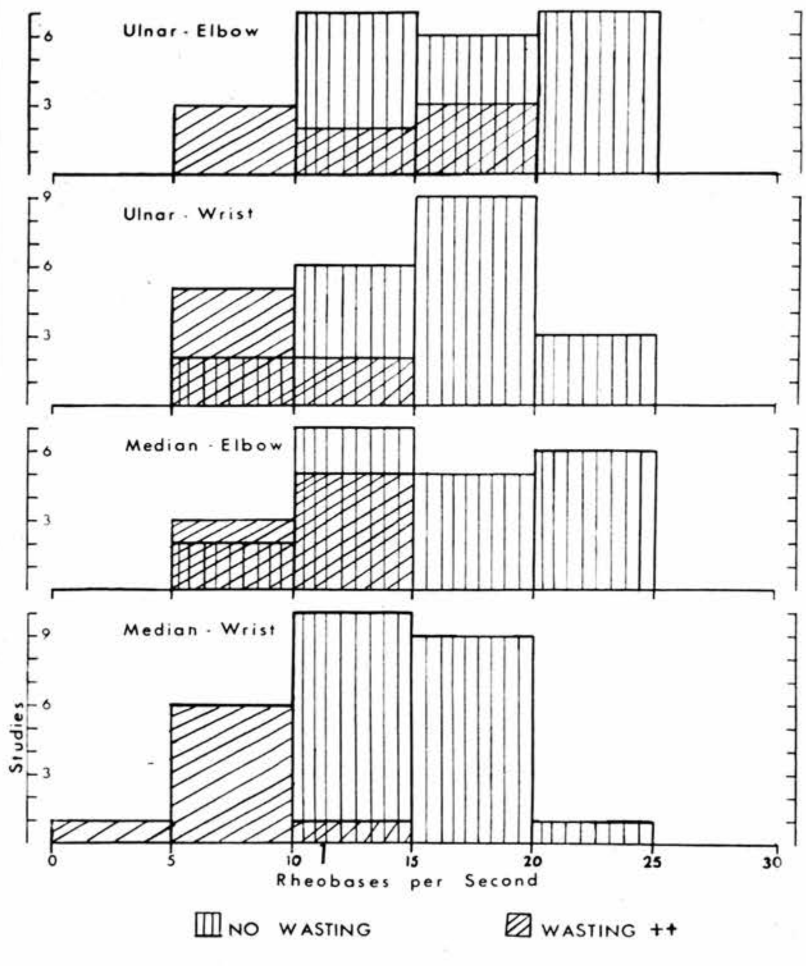

Ulnar - Elbow
Ulnar - Wrist
Median - Elbow
Median - Wrist
Studies
3
6
9
0
5
10
15
20
25
30
Rheobases per Second
NO WASTING
WASTING ++

FIG.12

FIGURE 12

Shows the distributions of the accommodation slope values among the patients with polyneuropathy (motor and 'mixed') with muscle wasting and among those without any wasting.

of the nerves in polyneuropathic patients complicated with muscle wasting.

In Table 23, the mean values of accommodation slopes obtained in the above two groups are compared. The Table shows that the group mean value of accommodation slope in the motor fibres was significantly lower in the majority of the nerves in the group of patients with more than minimal wasting of muscle than in those with minimal or no muscle wasting.

Correlation between accommodation, clinical course and prognosis : In clinical practice, a test of function may be used for the purposes of prognosis as well as for diagnosis. The data were re-examined to see whether there was any correlation between the accommodation changes and later recovery. In view of the findings mentioned earlier, cases of pure sensory polyneuropathy were excluded.

The patients who had an almost complete recovery or a marked improvement have been included in group 1 and those with slow recovery or none at all have been included in group 2. All of them were treated with steroids.

Tables 24 and 25 show the values of the slopes of accommodation in the motor fibres in the nerves of the individual subjects of these two groups. These values have been plotted in the form of a histogram for comparison

TABLE 23

COMPARISON OF MEAN ACCOMMODATION SLOPES FOR MOTOR FIBRES IN POLYNEUROPATHY WITH MUSCLE WASTING AND WITHOUT WASTING

Nerve	Side	Slope in rheobases per second		t	P	f
		Wasting -nil	Wasting + +			
Ulnar (Elbow)	Right	16.7 ± 1.3	12.9 ± 2.4	1.2	> 0.2	12
	Left	16.6 ± 1.2	12.1 ± 1.7	1.7	> 0.1	12
Ulnar (Wrist)	Right	15.8 ± 1.4	8.5 ± 1.8	2.6	< 0.05	12
	Left	15.5 ± 1.6	8.1 ± 1.7	2.7	< 0.05	12
Median (Elbow)	Right	16.4 ± 1.6	10.5 ± 1.0	2.2	< 0.05	12
	Left	15.8 ± 1.6	10.2 ± 1.3	2.1	> 0.05	12
Median (Wrist)	Right	14.9 ± 0.9	5.3 ± 0.2	5.0	< 0.001	12
	Left	14.6 ± 0.9	7.9 ± 1.8	3.3	< 0.001	12

TABLE 24

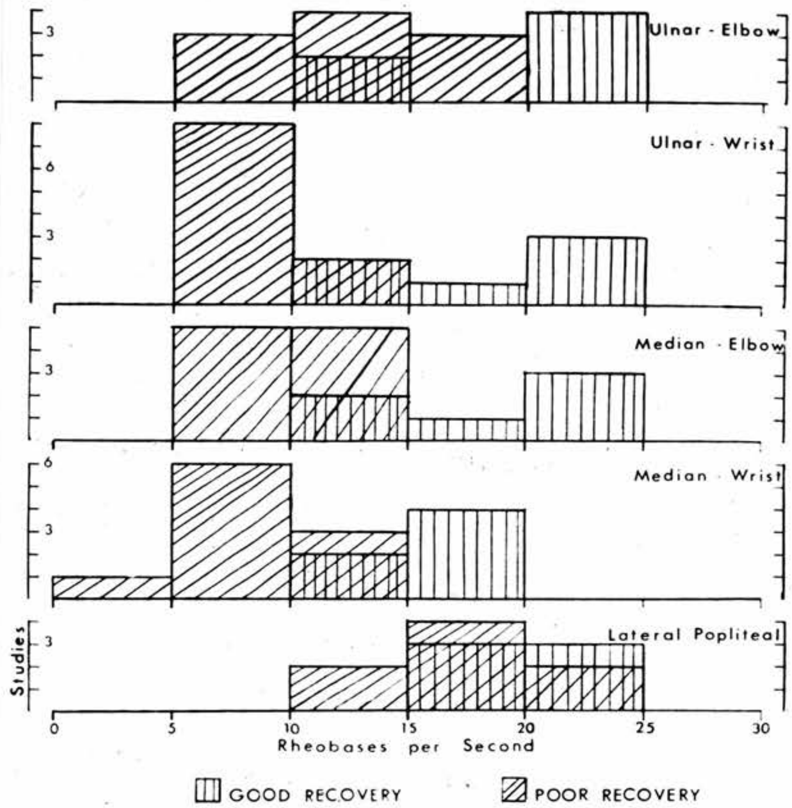
ACCOMMODATION SLOPES FOR MOTOR FIBRES IN POLYNEUROPATHY WITH GOOD RECOVERY

Case No.	Name	Side	Slope in rheobases per second				
			Ulnar		Median		Lat. Pop.
			Elbow	Wrist	Elbow	Wrist	
7017	M.Mc.	Right	22.0	20.0	20.0	24.0	18.3
		Left	20.0	19.8	24.2	17.2	22.3
7789	I.B.	Right	20.0	22.1	20.5	20.0	21.3
		Left	21.2	21.3	19.5	18.0	20.1
7233	E.C.	Right	13.3	13.3	12.5	13.2	18.1
		Left	13.1	12.0	11.8	10.8	17.5

TABLE 25

ACCOMMODATION SLOPES FOR MOTOR FIBRES IN POLYNEUROPATHY WITH SLOW OR NO RECOVERY

Case No.	Name	Side	Slope in rheobases per second				
			Ulnar		Median		Lat.Pop.
			Elbow	Wrist	Elbow	Wrist	
7070	T.F.	Right	10.0	6.0	12.0	6.0	—
		Left	9.0	6.4	10.5	7.5	—
6377	C.H.	Right	18.0	14.0	10.0	5.0	18.0
		Left	16.0	12.8	9.5	13.0	16.2
6558	J.P.	Right	10.0	8.0	9.1	12.0	21.5
		Left	12.8	8.3	6.7	15.0	24.0
7554	G.C.	Right	16.0	7.5	12.0	5.0	12.0
		Left	14.0	8.3	13.5	6.8	13.2
7042	M.M.	Right	7.5	6.6	8.2	5.2	17.3
		Left	9.4	5.2	7.5	4.4	18.2



Ulnar - Elbow
Ulnar - Wrist
Median - Elbow
Median - Wrist
Lateral Popliteal
Studies
3
6
0
5
10
15
20
25
30
Rheobases per Second
GOOD RECOVERY
POOR RECOVERY

FIG. 13

FIGURE 13

Shows the distributions of the accommodation slope values among the patients with polyneuropathy (motor or 'mixed') with good recovery and among those with slow or no recovery.

between the two groups (vide figure 13). The histogram shows that the distribution of comparatively smaller slope values was more common among the motor fibres of the patients of group 2 than among those of group 1.

Table 26 compares the mean accommodation slope for the motor fibres of the above two groups of polyneuropathies, The comparison reveals that there was a significantly lower group mean accommodation in the motor fibres of the median merve at elbow and at wrist and of the ulnar nerve at wrist in the patients with worse prognosis than in those with a better prognosis. The group mean slopes of accommodation for the motor fibres of the lateral popliteal nerve and the ulnar nerve at elbow were also smaller in the former group, but the differences in these were not statistically significant.

Discussion

In this study, accommodation of the motor fibres of the peripheral nerves was commonly found impaired in cases of polyneuropathy showing clinical evidence of motor involvement and also in cases of vitamin B_{12} deficiency neuropathy. Slowing of conduction has recently been recognised as one of the effects of pathological changes in motor fibres (Simpson, 1956; Henriksen, 1956). Measurement of conduction velocity is now being

TABLE 26

COMPARISON OF ACCOMMODATION SLOPES FOR MOTOR FIBRES IN POLYNEUROPATHY WITH GOOD RECOVERY AND WITH SLOW OR NO RECOVERY

Nerve	Side	Mean accommodation slope in rheobases per second		t	P	f
		Group 1	Group 2			
Ulnar (Elbow)	Right	18.4 ± 2.9	12.3 ± 1.9	1.9	>0.1	6
	Left	18.1 ± 2.5	12.2 ± 1.3	2.4	>0.05	6
Ulnar (Wrist)	Right	18.4 ± 2.7	8.4 ± 1.4	3.5	<0.05	6
	Left	17.7 ± 2.9	8.1 ± 1.3	3.4	<0.05	6
Median (Elbow)	Right	19.0 ± 3.4	10.2 ± 0.8	3.2	<0.05	6
	Left	18.5 ± 3.7	9.5 ± 1.2	3.0	<0.05	6
Median (Wrist)	Right	17.0 ± 2.1	6.6 ± 1.5	4.0	<0.01	6
	Left	15.3 ± 2.3	9.3 ± 2.0	1.8	>0.05	6
Lateral Popliteal	Right	19.2 ± 1.2	17.2 ± 1.9	0.8	>0.4	6
	Left	19.9 ± 1.6	17.9 ± 2.2	0.7	>0.4	6

used routinely in the diagnosis of peripheral nerve disease. Simpson (1962a,b) has pointed out that the accommodation of nerve is likely to be more vulnerable than its rate of conduction to alteration in the metabolism of the nerve cell and axon processes, but no observation has yet been reported on nerve accommodation in polyneuropathies. The diagnosis of polyneuropathy has often to be made entirely on clinical evidence where current electrophysiological tests give normal results. Measurement of the conduction velocity has no doubt been a great advance in the field of clinical neurology, but, on occasion, such measurement fails to reveal any retardation of the speed of conduction of the nerve impulse in patients with clinical features strongly suggestive of polyneuropathy. The present observation of impairment of accommodation, at least in some cases of motor polyneuropathy suggests that this measurement maybe of some help in the diagnosis of cases of motor or 'mixed' polyneuropathies, where clinical features and conduction velocity studies are inconclusive.

The results show that the impairment of accommodation in polyneuropathies was directly related to the degree of wasting of the muscles present. One of the factors determining the rate and degree of recovery from a neurological disorder is the site and mode of damage to the neurone. Marked wasting of muscles can only occur if there is denervation and not simply demyelination. Accordingly the correlation of the degree of impairment of accommodation with the state of muscle wasting and the poor prognosis observed in this study suggests that the process of accommodation is dependent on the integrity of the axon process itself. This is further suggested by the impaired accommodation noted in motor neurone disease (vide chapter 6).

This study also raises the possibility that the degree of impairment of accommodation may be an indication of the prognosis of the case; but further study is needed to substantiate this suggestion.

<u>Breakdown of accommodation</u> : 'Early breakdown' of accommodation observed in the fibres showing impaired accommodation suggests that the current strength necessary to cause 'breakdown' of accommodation is related to the degree of accommodation in a nerve. It may be mentioned here that the impaired accommodation noticed at the site of compression in compression neuropathy was also associated with 'early breakdown' of accommodation (vide chapter 4).

Presence of 'early breakdown' even in fibres with a normal accommodation in patients with polyneuropathy makes it likely that the breakdown of accommodation with a smaller current strength precedes alteration of the time constant of accommodation in nerve fibres.

Summary and Conclusions

The accommodation of the peripheral nerves was studied in patients with different clinical types of polyneuropathy.

The accommodation was found to be diminished in the motor fibres of the peripheral nerves in the patients with motor involvement and in those with vitamin B_{12} deficiency. The impairment of accommodation was more marked in patients with muscle wasting and poorer prognosis.

It is suggested that measurement of accommodation may profitably be used as one of the diagnostic techniques in certain selected groups of patients with polyneuropathy.

'Breakdown' of accommodation was constantly found at a lower current strength than normal in the nerve fibres with impaired accommodation. This 'early breakdown' was evident also in some of the nerves with a normal slope value in patients with polyneuropathy with involvement of motor nerve fibres. In view of these facts, it is likely that the 'point of breakdown' of accommodation in any nerve fibre is related to the degree of its accommodation and 'early breakdown' may be the first indication of a likely impairment of accommodation in a nerve fibre at a later date.

CHAPTER 6

STUDIES ON MOTOR NEURONE DISEASE

Selection of subjects

The cases were selected on the presence of the following features in each of them, but the extent of the abnormalities varied from case to case.

1. Wasting of muscles.
2. Presence of fasciculation.
3. Absence of any objective or subjective sensory disturbances.
4. Presence of electromyographic evidence of anterior horn cell damage.

Pyramidal tract involvement was evident in some of them.

Nerves studied

Accommodation was studied for the motor fibres of the ulnar and median nerves at elbow and at wrist of both sides in eight patients with motor neurone disease ('amyotrophic lateral sclerosis'). The method of study was the same as for the controls. Fifty-six estimations of accommodation in total were made on them.

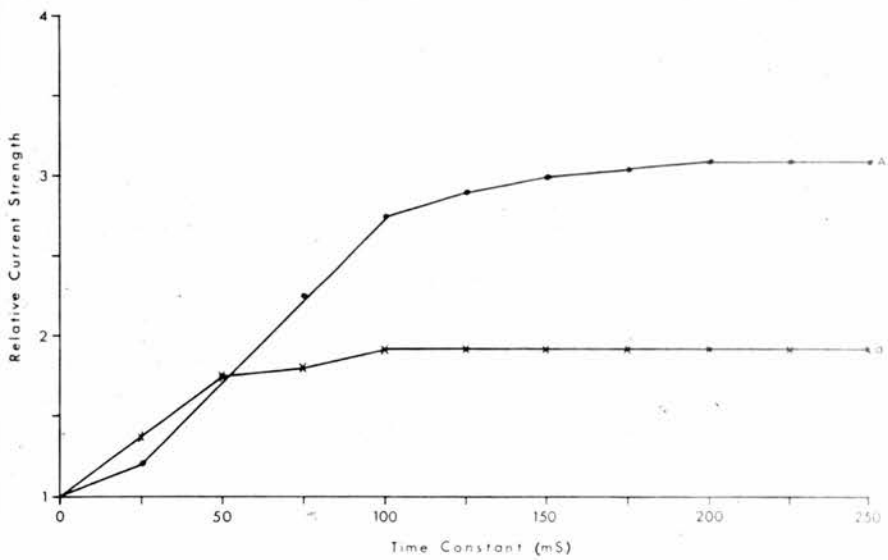

4
3
2
1
Relative Current Strength
A
0
50
100
150
200
250
Time Constant (mS)

FIG.14

FIGURE 14

Shows the accommodation curve for the ulnar nerve at elbow (a) from a patient with motor neurone disease (Case no. 7231). A curve for the same nerve at elbow (A) from a control subject is also shown for comparison. Slope values : (a) = 15.0 and (A) = 20.0 rheobases per second.

Results

Nature of the accommodation curves : The accommodation curves for the motor fibres of the nerves of these patients maintained the initial linearity of normal curves, but the slope of this linear part was flatter than normal for most of these nerves. One such curve has been reproduced in figure 14 which also contains a normal curve for the same nerve fibres.

The figure also shows that 'breakdown' of accommodation has occurred with a lower current strength in the motor fibres of the patient with motor neurone disease. This feature was constantly observed in the fibres having an accommodation slope value less than normal and was also frequently observed even in presence of a normal slope of the initial linear part.

Accommodation slope values : Table 27. shows the values of the accommodation slopes for the motor fibres obtained in the different nerves at different sites in the patients with motor neurone disease. The lesion in this disease is not symmetrical, consequently the slope values for a nerve in either limb have been shown as separate observations. Similarly, the group mean for a nerve has been calculated separately for each limb.

A review of Table 27. shows that in 32 of these 56

TABLE 27

ACCOMMODATION SLOPES FOR MOTOR FIBRES IN PERIPHERAL NERVES IN MOTOR NEURONE DISEASE

Case No.	Name	Side	Slope in rheobases per second			
			Ulnar		Median	
			Elbow	Wrist	Elbow	Wrist
4618	M.R.	Right	10.0	6.0	12.0	10.0
		Left	11.5	5.5	10.8	9.0
6735	J.Q.	Right	23.0	19.0	23.0	18.0
		Left	22.0	17.5	24.0	25.0
7065	E.H.	Right	11.4	10.0	12.2	7.0
		Left	10.8	5.0	10.0	9.0
7730	H.K.	Right	22.0	23.0	24.2	20.1
7231	E.C.	Right	15.0	14.4	14.5	14.0
7555	M.M.	Right	12.2	11.8	14.4	14.0
		Left	18.0	19.4	17.0	18.0
7294	A.B.	Right	20.3	21.4	22.6	22.0
		Left	21.0	21.0	22.2	22.8
7952	J.C.	Right	8.0	8.2	9.4	9.2
		Left	11.2	10.4	8.1	9.1

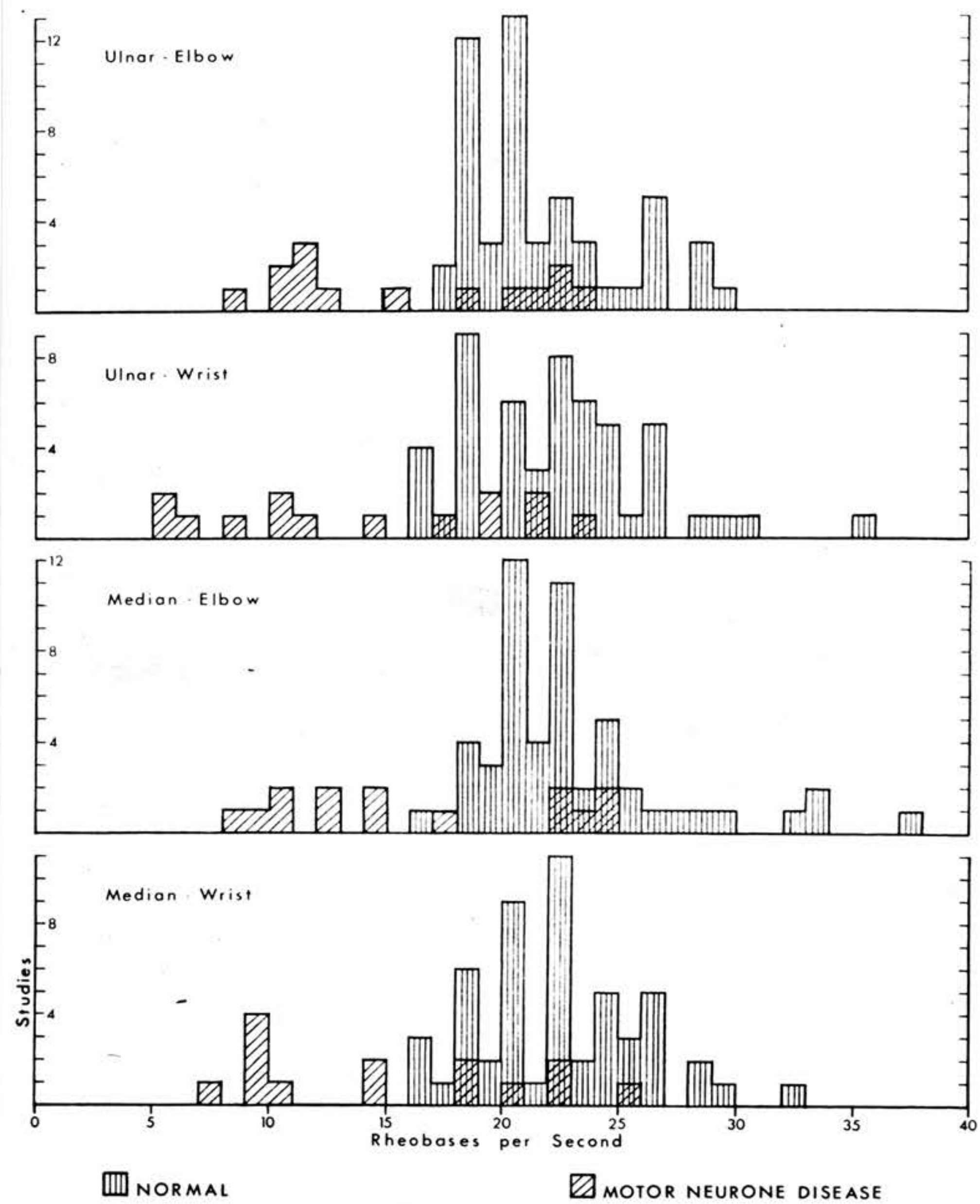

Ulnar - Elbow
Ulnar - Wrist
Median - Elbow
Median - Wrist
Studies
12
8
4
0
5
10
15
20
25
30
35
40
Rheobases per Second
NORMAL
MOTOR NEURONE DISEASE

FIG.15

FIGURE 15

Shows the distributions of the accommodation slope values for the different nerves among the patients with motor neurone disease and among the normals (controls).

studies the accommodation slopes were at or below 16 rheobases per second, the lowest value obtained in the controls. An inspection of figure 15 would also reveal this preponderance of smaller slope values for the motor fibres of the nerves in the patients with motor neurone disease. In three of the patients, twenty studies were carried out and all gave slopes for accommodation curves for the motor fibres within normal range. In another patient, the four studies carried out on the left arm were within the normal range whereas the four on the other side gave lower slopes than the controls. The disability in this particular patient started initially in the left side.

The mean values of the slopes for the motor fibres of the two nerves at elbow and at wrist are compared with the mean values of the controls in Table 28.

An analysis of the mean values reveals that in the patients with motor neurone disease the motor fibres of both ulnar and median nerves have a diminished accommodation compared with the controls. This difference was statistically significant.

Discussion

The significantly diminished accommodation in motor fibres observed in the present study in motor neurone disease is an interesting phenomenon. Depression of the rheobase and abnormal chronaxie of peripheral nerves have

TABLE 28

COMPARISON OF MEAN ACCOMMODATION SLOPES FOR THE MOTOR FIBRES IN MOTOR NEURONE DISEASE AND IN CONTROLS

	Slope in rheobases per second					
Nerves	Control		M.N.D.	t	P	f
Ulnar (Elbow)	21.3 ± 0.4	Right	15.3 ± 2.0	4.6	<0.001	58
		Left	15.7 ± 2.1	4.0	<0.001	56
Ulnar (Wrist)	22.0 ± 0.5	Right	14.2 ± 2.2	4.7	<0.001	58
		Left	13.1 ± 2.8	4.9	<0.001	56
Median (Elbow)	22.6 ± 0.6	Right	16.5 ± 2.0	3.5	<0.001	58
		Left	15.3 ± 3.0	3.6	<0.001	56
Median (Wrist)	22.0 ± 0.5	Right	14.3 ± 1.9	5.1	<0.001	58
		Left	15.5 ± 3.8	3.8	<0.001	56

been reported in this state (Arieff, Dobin & Tigay, 1957).

Repetitive responses of muscles to stimulation of a motor nerve have also been reported in motor neurone disease (Drechsler, 1957; Simpson, 1962a; Polini & Sala, 1962). Liberson & Pavasars (1960) suggested that these repetitive discharges might be due to either different rates of conduction in the different fibres of the same nerve or to repetitive firing of the same nerve fibre. As mentioned in a previous chapter, Katz (1937) concluded that accommodation was an important factor controlling the duration of excitability of a nerve fibre during the passage of a stimulus. Kugelberg & Taverner (1950) have mentioned that the double discharges observed on electrical stimulation of a peripheral nerve in motor neurone disease were similar to those obtained in tetany, a condition associated with impaired accommodation in peripheral nerves.

Although the mean values of accommodation derived from the present group of patients with motor neurone disease were significantly lower than the control values, an analysis of the individual cases of this series shows that the accommodation value was not invariably lower than the range of the controls. The values obtained in case nos. 6735, 7730 and 7294 are such examples. Repetitive discharges are also not invariably found in motor neurone disease. None of the electrical phenomena said to be characteristic of motor neurone disease are constantly observed in all patients (Dobin, Arieff & Tigay, 1960). This may be due to the slowly progressive nature of the pathological changes.

Correlation between fasciculation and impaired accommodation : Fasciculation is an invariable phenomenon in motor neurone disease. Fasciculation is also observed in hypocalcaemia, a condition associated with impaired accommodation. Hence, the observation that accommodation may be impaired in motor neurone disease prompted the author to examine the possibility of impaired accommodation playing a role in the production of fasciculation. This possible correlation is further suggested by the fact that conditions like cooling, hyperventilation, etc. which are known to impair accommodation also increase fasciculation (Denny-Brown & Pennybacker, 1938; Swank & Price, 1943).

The mechanism of production of fasciculations in motor neurone disease remains unknown. Denny-brown & Pennybacker (1938) concluded that the fasciculations observed in 'amyotrophic lateral sclerosis' were due to the spontaneous activity of individual motor units. On the basis of this conclusion, they suggested that the production of the impulse for the abnormal contraction of the muscle fasciculi must be related to the pathological changes either in the anterior horn cells or in the motor nerves themselves.

Grund (1938) and later Sheldon & Woltman (1940) failed to abolish fasciculations in patients with 'amyotrophic lateral sclerosis by spinal anaesthesia with intrathecal Procaine and they concluded that the anterior horn cells had no role to play in the production of fasciculation. Swank & Price (1943) confirmed these findings, but they also noticed abolition or reduction of fasciculations in the corresponding muscles following blocking of the anterior tibial or ulnar nerves. They concluded that the stimuli provoking fasciculations in motor neurone disease were derived mainly from the peripheral nerve fibres. As they observed some reduction, although no complete abolition, in some of their patients with spinal anaesthesia, they further concluded that in advanced cases anterior horn cells may play some part as well, in its production. Odom, Russel & McEachern (1943) observed that blocking a peripheral nerve caused a decrease in the degree of fasciculations in 2 of their 6 patients with motor neurone disease and no change in another 4. De Jong & Simons (1942) on the other hand failed to modify the existing fasciculations by peripheral nerve block in such cases. Forster & Alpers (1944) did not observe any reduction of fasciculations following blocking of the lateral popliteal nerve or spinal anaesthesia in their patients with motor neurone disease and concluded that fasciculations do not originate in the anterior horn cells, but in the region of the myoneural junction.

Swank & Price (1943) classified motor neurone disease into rapidly progressive and slowly progressive types. They suggested that, in the former a large part of the neurone especially its distal portion, appears to be affected, whereas in the latter, the disturbance appears to be limited to or more marked near the termination of the nerve fibre.

The conflicting results obtained by peripheral nerve block and spinal anaesthesia on fasciculations in motor neurone disease point to the possibility that the spontaneous discharges may arise at a number of sites along the neurone. These factors may vary from case to case depending upon the severity of the pathological lesion. The impaired accommodation observed in the present study in a proportion of patients with motor neurone disease supports the suggestion that spontaneous firings may occur from peripheral parts of the neurone and hence that fasciculation may arise peripherally though not necessarily exclusively so. This may explain the reduction or even abolition of fasciculations observed by some authors following nerve block.

However, it is not justifiable to incriminate impaired accommodation as the sole cause for the production of fasciculation. The absence of impaired accommodation in some of the cases studied may be due to the progress of the case and the distribution of the predominant lesion. Of the cases showing normal accommodation in the present series, one (case no. 6735) had a very slowly progressive course and in another (case no. 7294) the disease was limited clinically to the bulbar region. She had no clinical evidence of involvement of lower motor neurones to the limbs. No fasciculation was visible clinically excepting in the tongue, but electromyography showed fasciculation in the limb muscles.

The above observations prompt the author to suggest the possibility, at least in some cases, that impaired accommodation may, in conjunction with other factors, help in the production of fasciculations in motor neurone disease. Impaired accommodation promotes repetitive discharges in the damaged nerve in response to normal or abnormal impulses leading to rhythmic contraction of motor units. This mechanism also explains the exacerbation or provocation of fasciculations by 'voluntary or electric stimulation' as mentioned by Duchenne (Denny-Brown, 1938).

It must be made clear however, that this work does not suggest that impaired accommodation is an invariable accompaniment of fasciculation. The present experiments were not however, concerned with the investigation of the mechanism of fasciculation.

Breakdown of accommodation : The possible relation of 'point of breakdown' of accommodation in a nerve fibre with its degree of accommodation suggested in the preceding chapter (chapter 5) is supported by the observation of 'early breakdown' in the motor fibres of the patients with motor neurone disease.

SUMMARY AND CONCLUSIONS

The property of accommodation in the motor fibres of the peripheral nerves has been studied in a group of patients with motor neurone disease.

Accommodation was found to be impaired in these fibres in most of these patients. Early 'breakdown' of accommodation was an invariable phenomenon in the motor fibres with impaired accommodation. It was also observed in many of these fibres even in presence of a normal accommodation. These observations on the 'breakdown' of accommodation were similar to those encountered in other diseases associated with impairment of accommodation in the motor fibres and support the suggestions made in chapter 5.

The present knowledge on the mechanism of fascicul-ation in motor neurone disease has been discussed. It is suggested that fasciculations in motor neurone disease are produced by the action of multiple factors and that impaired accommodation is possibly one of these, at least in some of the cases.

CHAPTER 7

GENERAL SUMMARY AND CONCLUSIONS

The concept of the phenomenon of accommodation in the peripheral nerve fibres has been discussed. The evolution of the present knowledge on this phenomenon and the different theories put forward to explain its physiological basis have been considered. The factors known to affect this property in a nerve fibre have been mentioned.

It has been pointed out that very few studies have been carried out to investigate the phenomenon of nerve accommodation in human beings, both normal and pathological.

The purpose of carrying out the studies incorporated in this thesis has been explained.

The details on the above points constitute the introductory chapter (chapter 1).

In chapter 2, the method of measuring accommodation adopted for this study has been described. This includes a brief description of the stimulator used and details of the methods of stimulus application, of drawing the accommodation curves and of expressing accommodation quantitatively.

Other methods available for studying accommodation in nerves have been mentioned and reasons for employing the present procedure explained in the same chapter.

In chapter 3, measurements of accommodation carried out in the motor fibres of a group of control subjects having no evidence of peripheral nerve lesion have been reported and discussed.

On the basis of the accommodation values obtained in the present work on the controls and the values reported by other workers, it has been concluded that the calculated value of accommodation depends upon the experimental procedure and, for comparative studies, a standardised procedure should be adopted.

No difference could be established in the capacity of accommodation in the motor fibres between the ulnar and median nerves in control subjects in this study, but faster accommodation (i.e. a lower time-constant of accommodation) was observed in the motor fibres of the lateral popliteal nerve than in the motor fibres of the ulnar and median nerves.

No regional difference in the capacity of accommodation along the length of a normal nerve could be detected by the method used.

The breakdown of accommodation was detected in the motor fibres at a strength of 2 - 4 times the rheobasic under normal circumstances.

Impaired accommodation in the motor fibres was noted in patients with compression neuropathy, polyneuropathy and motor neurone disease (vide chapters 4, 5 and 6). None of these observations has been reported before.

Impaired accommodation has been suggested as the reason for obtaining repetitive firing in compressed nerves after a single stimulus. Arguments have been put forward that impaired accommodation, however, may not be the only factor in determining the occurrence of repetitive firings in general (vide chapter 4).

In chapter 5, the limitations of measurement of the velocity of conduction as a diagnostic tool in the diagnosis of peripheral nerve lesion have been pointed out and it has been suggested that, as accommodation of a nerve fibre depends more directly upon its oxidative metabolism, it may be used as one of the diagnostic techniques in certain selected patients with polyneuropathy where conduction velocity studies fail to show any abnormality. The value of the method is that changes in accommodation are related to abnormalities of the axon, rather than of the myelin sheath as in disorders of conduction velocity.

In patients with polyneuropathy, the impairment of accommodation in the motor fibres was found to be directly related to the degree of associated muscle wasting. A probable similar relationship was observed between the degree of impairment of accommodation and the rate of recovery in these patients, a greater impairment having been observed in the motor fibres of many of their nerves in patients with slow or no recovery (vide chapter 5).

In chapter 6, the controversy on the mechanism of fasciculation in motor neurone disease has been discussed and it has been suggested that impaired accommodation may be one of the many factors responsible for the production of fasciculation in this condition.

The motor fibres with impaired accommodation were observed to have 'early breakdown' of accommodation, suggesting that the point of 'breakdown' of accommodation is probably directly related to the degree of accommodation in a nerve fibre. This 'early breakdown' of accommodation was also noticed in many of the motor fibres with a normal accommodation, among the patients with compression neuropathy, polyneuropathy and motor neurone disease. On the basis of the observed impairment of accommodation in motor fibres in these diseases, it has been suggested that 'early breakdown' of accommodation may be one of the earlier indications of its subsequent impairment (vide chapters 4, 5 and 6).

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